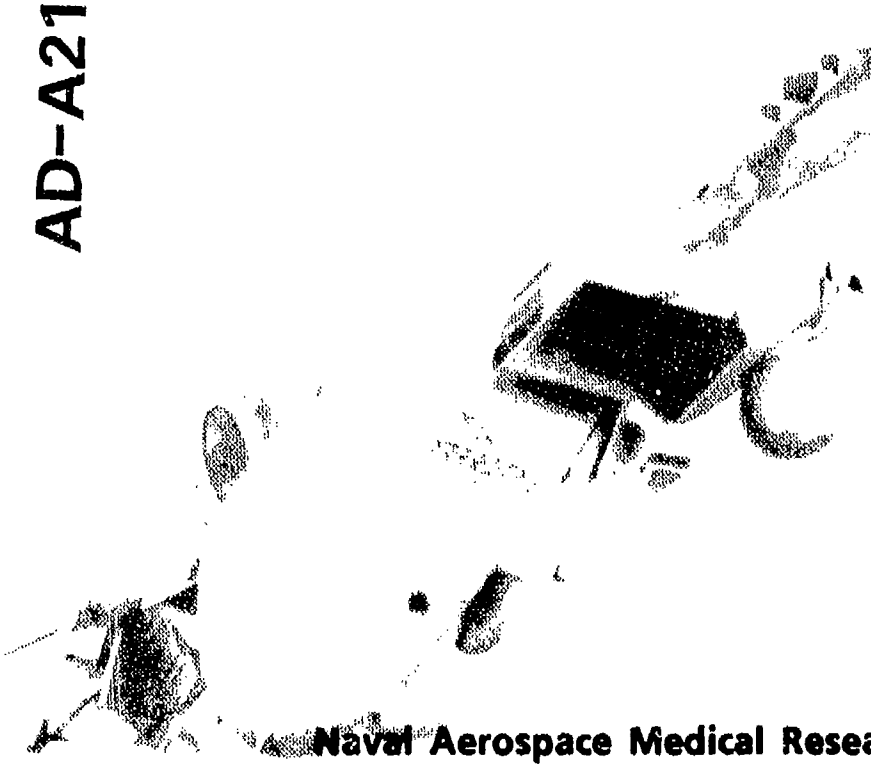
TRIAZOLAM: AN ABSTRACTED BIBLIOGRAPHY

G.G. Reams and W.A. Morey



Naval Aerospace Medical Research Laboratory
Naval Air Station
Pensacola, Florida 32508-5700

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James A. Brady

J. A. BRADY, CAPT, MSC USN
Commanding Officer

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19. ABSTRACT (Continue on reverse if necessary and identify by block number)

This document is composed of a group of abstracts derived from selected research articles on the drug triazolam. The abstracts are in alphabetical order, according to the last name of the first author. Each abstract includes the author(s) names(s), the title of the article, the source of publication, and the drugs and dosages used. These are followed by a brief description of the subjects and the procedures used. A summary of the research findings and discussion is included, along with a list of relevant keywords. A subject index is included at the end of the document to facilitate locating articles that deal with specific subjects. Keywords

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PREFACE

The Naval Aerospace Medical Research Laboratory is engaged in an effort to determine the effects on performance of several commonly used therapeutic drugs. These investigations, combined with clinical research reports and the experience of our senior flight surgeons, establish the foundation for judging the potential impact of any specific drug treatment on safety of flight and operational readiness. This bibliography focuses on a group of drugs called benzodiazepines, which are operationally used as sleep-inducing agents. The abstracted bibliography is designed as a working document reflecting a literature search and establishes the basic material for a literature summary.

In addition, articles are included that contain information related to the broad topic of human performance. Selected areas of priority under the "clinical-performance" heading include visual, auditory, vestibular, cardiopulmonary, musculoskeletal, and psychological systems. References pertaining to biochemistry and pharmacodynamics are included as considered necessary to understand certain aspects of research design.

The printing format was selected to provide the user with the option of using this publication as a book or as a supplement to a card file. All abstracts can be torn out and filed.

We have chosen a printing format, tear-out 5 x 8 index cards, to reflect our emphasis on producing a versatile working document, which can be supplemented with future abstracts. A topic-area index is provided at the end of the monograph. The topic-area descriptions for each abstract can be found at the bottom of each 5 x 8 card and represent three general areas: drug, (each specified drug is listed), biomedical discipline (general topic area of the report), and subject population (human or nonhuman).

A numerical filing system can be found at the top right side of each 5 x 8 card. The numerical system corresponds to an alphabetical order by author. This initial volume uses numerical intervals of 10, which will allow abstracts from future volumes to be merged while still retaining a numerical and alphabetical order. Only English-language articles or those with an English-language summary are included.

Each abstract contains eight sections of information: Authors, Title, Reference, Drugs (including dosages when feasible), Subjects (number and type), Procedures (brief general description), Findings (brief listing of major findings), and Index (the topic-area index). In some cases, it was necessary to use more than one 5 x 8 card to adequately abstract the article.

ACKNOWLEDGMENTS

We gratefully acknowledge Mrs. Nell R. Davis and Mrs. Elaine Cotton for their conscientious technical and secretarial skills. Furthermore, we would like to express our sincere indebtedness to Carla Brown, who superbly managed this project and kept it on schedule. Moreover, we sincerely appreciate the valuable editorial contributions of Kathleen S. Mayer.

10

AUTHORS: Adam, K., Oswald, I., and Shapiro C.

TITLE: Effect of Loprazolam and of Triazolam on Sleep and Overnight Urinary Cortisol

REFERENCE: Psychopharmacology, Vol. 82, pp. 389-394, 1984.

DRUGS: Loprazolam 0.5-1.0 mg
Triazolam 0.5 mg

SUBJECTS: Human - 9

PROCEDURES: A crossover design, which used a washout period. EEG and EOG were recorded, coded, and scored blind.

FINDINGS: The first non-drug night rebound insomnia was reported severe for triazolam; however, both drugs produced a rebound effect. Triazolam (0.5 mg) is too large a dose for most patients (especially elderly).

INDEX: Triazolam, Benzodiazepines - Psychology - Human

20

AUTHORS: Alexander, N., Baldwin, R.J.J., Cranfield, R., Hughes, D., Khan, G.U., and Venugopal, S.S.

TITLE: Comparison of Triazolam (Halcion) and Flurazepam (Dalmane) for the Treatment of Insomnia in General Practice

REFERENCE: Clinical Trials Journal, Vol. 21, No. 6, pp. 371-377, 1984.

DRUGS: Triazolam 0.25 mg
Flurazepam (FM) 15 mg

SUBJECTS: Human - 80

PROCEDURES: A prospective double-blind clinical study of insomniacs, using subjective measurements for time of induction and quality of sleep.

FINDINGS: Triazolam was better than flurazepam in sleep induction and morning-after alertness, and presented a lower incidence of morning hangover.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

30

AUTHORS: Anonymous

TITLE: Triazolam (Halcion): Psychological Disturbances

REFERENCE: Drug and Therapeutic Bulletin, Vol. 17, No. 19, p. 76, 1979.

DRUGS: Triazolam (0.5-1 mg)

SUBJECTS: Human - 4 long-term insomniacs

PROCEDURES: A brief report.

FINDINGS: The four patients developed psychological changes such as anxiety, depersonalization, feeling of reality, paranoia, restlessness, hyperacusis, altered smell and taste, and paresthesia. After an additional 600 reports of suspected reactions were submitted, the Dutch government suspended the use of the drug.

COMMENT: The bulletin recommended that the maximal dosage should be 0.25 mg. No further circumstances were given.

INDEX: Triazolam - Psychology, Acoustics, Vestibular - Human

40

AUTHORS: Barclay, W.R., Curran, W.J., Greenblatt, D.J., Lapierre, Y., O'Donnell, T.J., Ayd, F.J., Callan, J.P., Gardner, E.A., Ladimer, I., Lehmann, H.E., van Praag, H.M., and Shader, R.I.

TITLE: Behavioral Reactions to Triazolam

REFERENCE: Lancet, Vol. 2, No. 8150, p. 1018, 1979.

DRUGS: Triazolam 0.25 or 0.50 mg
Flurazepam 15 or 30 mg

SUBJECTS: Human - 5000

PROCEDURES: Double-blind controlled trials using the two (above) drugs and placebo.

FINDINGS: Side effects of triazolam were equal to or less than those of flurazepam.

COMMENT: The article implies that the research was designed to determine whether the adverse effects reported in the Netherlands were of concern in the U.S. or if they were due to the much larger dosages employed there. The article assumes the latter.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

AUTHORS: Bentel, H.

TITLE: A Comparative Study Between Two New Benzodiazepine Hypnotics

REFERENCE: South African Medical Journal, Vol. 57, p. 769, 1980.

DRUGS: Flunitrazepam 2.0 mg
Triazolam 0.5 and 1.0 mg

SUBJECTS: Human - 120 (night before surgery)

PROCEDURES: Patients were divided into 3 groups of 40 each.

FINDINGS: Both substances proved to be active and resulted in the patients experiencing better sleep. Triazolam (0.5 mg) induced sleep in 65% of patients within 30 min. The corresponding figures for triazolam (1.0 mg) and flunitrazepam (2.0 mg) were 60% and 55%, respectively. Flunitrazepam (2.0 mg) had a pronounced soporific action on the trial population, and the majority of patients slept longer than 8 h.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

AUTHORS: Bliwise, D., Seidel, W., Karacan, I., Mitler, M., Roth, T., Zorick, F., and Dement, W.

TITLE: Daytime Sleepiness as a Criterion in Hypnotic Medication Trials: Comparison of Triazolam and Flurazepam

REFERENCE: Sleep, Vol. 6, No. 2, p. 156, 1983.

DRUGS: Triazolam 0.5 mg
Flurazepam 30 mg

SUBJECTS: Human - 24 (insomniacs)

PROCEDURES: Sleep lab, hypnotic medication trials typically determine efficacy by examining changes in polysomnographically recorded sleep. The authors introduce the use of daytime sleepiness, as assessed by the Multiple Sleep Lab Test (MSLT), used as a criterion for daytime functioning.

FINDINGS: Medications had virtually indistinguishable nocturnal effects but differed dramatically during the day. Flurazepam decreased sleep latency on the MSLT, whereas triazolam did not. Results could indicate that daytime sleepiness is a concomitant effect of flurazepam.

COMMENT: The study implies that flurazepam has a greater effect on performance than triazolam, at least in reference to arousal.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

70

AUTHORS: Blumenthal, M., Byring, R., and Koivula, K.

TITLE: Comparison of Nitrazepam 5 mg with Triazolam 0.5 mg in Young Psychiatric Insomniac Inpatients

REFERENCE: Acta Psychiatrica Scandinavia, Vol. 62, pp. 519-524, 1980.

DRUGS: Triazolam 0.5 mg
Nitrazepam 5 mg

SUBJECTS: Human - 60

PROCEDURES: A double-blind crossover design was used for the 2-day study. All subjects received triazolam the first night followed by nitrazepam the second night.

FINDINGS: Both drugs decreased sleep latency and the number of awakenings, and increased the duration of sleep. Compared with nitrazepam, triazolam-treated patients slept longer, fell asleep faster, and had less nocturnal awakenings.

COMMENT: All data were collected subjectively, that is, the patients themselves evaluated their number of awakenings, number of minutes to go to sleep, et cetera, rather than investigator determining the actual time experimentally.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

80

AUTHORS: Boissl, K., Dreyfus, J.F., and Delmonte, M.

TITLE: Studies on the Dependence-inducing Potential of Zopiclone and Triazolam

REFERENCE: International Pharmacopsychiatry, Vol. 17, No. 2, pp. 242-247, 1982.

DRUGS: Triazolam (TM) 0.25 mg
Zopiclone (ZN) 3.75 mg

SUBJECTS: Human - 40

PROCEDURES: The randomized double-blind study used detoxified chronic alcoholics as subjects. Patients were given one of the drugs each time they felt a desire for alcohol. Patients were then evaluated for any special desire for the drug.

FINDINGS: Zopiclone is a non-benzodiazepine hypnotic. None of the volunteers developed a desire for ZN after the study, which suggests a lack of euphoria with this drug.

COMMENT: Suggests that ZN has less abuse potential than TM.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

AUTHORS: Bonnet, M.H.

TITLE: Effect of Sleep Disruption on Sleep, Performance, and Mood

REFERENCE: Sleep, Vol. 8, No. 1, pp. 11-19, 1985.

DRUGS: None

SUBJECTS: Human - 11

PROCEDURES: Normal subjects were used; sleep was frequently interrupted for 2 nights. Sleep stages, latency, and arousal times were measured. The Clyde Mood Scale, reaction time tasks, and the digit symbol substitution tests were administered.

FINDINGS: Periodic disruption of sleep rapidly degrades performance and results in impaired performance. "...there is a significantly altered distribution of sleep stages. Highly significant decreases in sensitivity to the auditory arousing stimulus were demonstrated."

INDEX: Psychology, Audiology - Human

AUTHORS: Borbely, A.A., Loepfe, M., Mattmann, P., and Tobler, I.

TITLE: Midazolam and Triazolam: Hypnotic Action and Residual Effects After a Single Bedtime Dose

REFERENCE: Arzneimittel-Forschung Drug Research, Vol. 3, No. 11, pp. 1500-1502, 1983.

DRUGS: Midazolam 7.5 or 15 mg
Triazolam 0.25 or 0.5 mg

SUBJECTS: Human - 15

PROCEDURES: The hypnotic action and residual effects of a single bedtime dose were investigated. Motor activity was continuously recorded by a wrist-worn activity monitor.

FINDINGS: Both compounds reduced nighttime motor activity in the first half but not in the second half of sleep. Subjects rated their sleep as more quiet. Performance in the morning, as measured by a psycho-motor test, was significantly impaired only after triazolam (0.5 mg). Rebound insomnia was absent in the 3 nights following drug intake.

COMMENT: Triazolam-mediated sleep affects psychomotor performance the following morning.

INDEX: Triazolam, Benzodiazepines - Psychology - Biomedical - Human

AUTHORS: Bowen, A.J.

TITLE: Comparative Efficacy of Triazolam, Flurazepam and Placebo in Out-patient Insomniacs

REFERENCE: Journal of International Medical Research, Vol. 6, pp. 337-342, 1978.

DRUGS: Triazolam (TZ) 0.5 mg
Flurazepam (FZ) 15 and 30 mg

SUBJECTS: Human - 120 (insomniacs)

PROCEDURES: Each patient was studied for 2 nights using a double-blind crossover design.

FINDINGS: Triazolam (0.5 mg) was superior to FZ (30 mg) in speeding sleep onset, increasing sleep duration, and reducing the number of nighttime awakenings. Triazolam (0.25 mg) was preferred to FZ (15 mg) and was significantly better than FZ on all sleep questions. Triazolam (0.25 mg) was preferred by more patients than FZ (30 mg) and was judged equally efficacious on individual sleep questions. Reports of side effects were minimal for both drugs. One patient reported blurred vision, one reported chest pressure, and another reported restlessness.

INDEX: Triazolam, Benzodiazepines - Vision, Psychology - Human

AUTHOR Carskadon, M.A., Seidel, W.F., Greenblatt, D.J., and Dement, W.C.

TITLE: Daytime Carry-over of Triazolam and Flurazepam in Elderly Insomniacs

REFERENCE: Sleep, Vol. 5, No. 4, pp. 361-371, 1982.

DRUGS: Triazolam (TZ) 0.25 mg
Flurazepam (FZ) 15 mg

SUBJECTS: Human - 13 (elderly insomniacs)

PROCEDURES: Total sleep and daytime sleepiness, using the Multiple Sleep Latency Test (MSLT) and Stanford Sleepiness Scale (SSS), as well as performance and mood (profile of mood states POMS), were all measured on 5 consecutive days.

FINDINGS: Sleep time was increased approximately 1 h in both drug groups. The MSLT showed increased sleepiness with FZ and decreased sleepiness with TZ. Vigilance was impaired with FZ and unchanged with TZ. Other performance tests showed slight improvement or no change. Mood tended to be improved with FZ and unchanged with TZ.

COMMENT: Findings suggested that FZ causes a significant residual sedation, and TZ improves daytime alertness. Neither compound had a significant effect on nocturnal respiration.

INDEX: Triazolam, Benzodiazepines - Psychology, Vision - Human

130

AUTHORS: Chatwin, J.C. and Johns, W.L.

TITLE: Triazolam: An Effective Hypnotic in General Practice

REFERENCE: Current Therapeutic Research, Vol. 21, No. 2, pp. 207-214, 1977.

DRUGS: Triazolam 0.25-1.0 mg

SUBJECTS: Human - 30

PROCEDURES: Patients were started on 0.25 mg with an option to increase the dose from the third through the seventh nights, if needed. Subjective measurements of quality of sleep were recorded. A double-blind crossover design was used.

FINDINGS: Mild side effects were reported by four patients. Eight patients required increased doses. The vast majority (27/30) of patients stated improvements in quality and quantity of sleep and reported minimal side effects.

COMMENT: An early clinical study was conducted prior to the product's introduction.

INDEX: Triazolam - Psychology - Human

140

AUTHORS: Chick, J.

TITLE: Hypnotics and Hangover

REFERENCE: British Medical Journal, Vol. 280, p. 1322, 1980. (letter to the editor).

DRUGS: Triazolam

SUBJECTS: N/A

PROCEDURES: A brief precautionary comment on the use of benzodiazepines.

FINDINGS: A patient should be advised not to medicate himself when his cognitive processes may already be disturbed by a recent dose of another hypnotic or to subject himself to yet further hangover the following morning.

INDEX: Triazolam - Psychology - Human

150

AUTHORS: Church, M.W. and Johnson, L.C.

TITLE: Mood and Performance of Poor Sleepers During Repeated Use of Flurazepam

REFERENCE: Psychopharmacology, Vol. 62, pp. 309-316, 1979.

DRUGS: Flurazepam 30 mg

SUBJECTS: Human - 12

PROCEDURES: A double-blind study to investigate performance effects using a four-choice reaction time task and the digit symbol substitution test (DSST) on poor sleepers over a 10-d period. Short-term memory was also measured.

FINDINGS: "Flurazepam had no significant effect on mood...."
"Flurazepam significantly impaired performance on a four-choice reaction time task and the DSST but not on a short-term memory test."

COMMENT: "Performance impairment on DSST showed a drug tolerance effect across the ten day drug period, but reaction time task showed no tolerance effect."

INDEX: Benzodiazepines - Psychology - Human

160

AUTHORS: Cobden, I., Record, C.O., and White, R.W.B.

TITLE: Fatal Intrahepatic Cholestasis Associated with Triazolam

REFERENCE: Postgraduate Medicine Journal, Vol. 57, pp. 730-731, 1981

DRUGS: Triazolam 0.25 mg

SUBJECTS: Human-case study of a 44-year-old man

PROCEDURES: The patient arrived at an emergency room.

FINDINGS: The patient developed severe pruritus with jaundice, which subsequently proved fatal. Liver histology showed intense cholestasis, but at postmortem, the bile ducts were patent and there was no cirrhosis. The findings were consistent with a cholestatic drug reaction. The most likely precipitant was the benzodiazepine triazolam, and surveillance was indicated for any further reactions to this recently (at that time) marketed hypnotic.

INDEX: Triazolam - Human

170

AUTHORS: Cohn, J.B.

TITLE: Double-blind Crossover Comparison of Triazolam and Lorazepam in the Posthypnotic State

REFERENCE: Journal of Clinical Psychiatry, Vol. 45, No. 3, pp. 104-107, 1984.

DRUGS: Lorazepam 2 mg
Triazolam 0.5 mg

SUBJECTS: Human - 30 (insomniacs)

PROCEDURES: Baseline (3-7 d).
Treatment periods (3-4 d).
Washouts between trial treatments (3 d).
A sleep questionnaire, the Stanford Sleepiness Scale, and a cognitive battery were administered to evaluate drug effects.

FINDINGS: Triazolam subjects slept better, got to sleep faster, awoke less, and had less drowsiness the following morning.

COMMENT: Triazolam (0.5 mg) was not significantly different than the control statistically, when comparing alertness the next morning. Others have suggested that such doses of triazolam will produce marked side effects. Self-evaluative reports may be questionable.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

180

AUTHORS: Committee on the Review of Medicines

TITLE: Systematic Review of the Benzodiazepines

REFERENCE: British Medical Journal, Vol. 280, No. 6218, pp. 910-912, 1980.

DRUGS: Benzodiazepines

SUBJECTS: N/A

PROCEDURES: N/A

FINDINGS: The addiction potential of benzodiazepines appears to be low. Long-acting (over 10 h) benzodiazepines should not be used if daytime performance is a factor. None should be used for primary treatment of anxiety or other psychiatric disorders. "The absence of posthypnotic effects or daytime sedation [of short 1/2 life compounds] is dose dependent...."

INDEX: Triazolam, Benzodiazepines - Psychology - Human

190

AUTHORS: Cordingley, G.J., Dean, B.C., and Harris, R.T.

TITLE: A Double-blind Comparison of Two Benzodiazepine Hypnotics, Flunitrazepam and Triazolam in General Practice

REFERENCE: Current Medical Research and Opinion, Vol. 8, No. 10, pp. 714-719, 1984.

DRUGS: Flunitrazepam (FM) 1 mg
Triazolam (TM) 0.25 mg

SUBJECTS: Human - 312

PROCEDURES: Subjects with sleep disorders requiring treatment were used in a double-blind study (7-14 nights). Data were collected by investigator assessment and patient assessment (regarding sleep).

FINDINGS: Six patients receiving FM and eight patients receiving TM withdrew from study because of side effects. A list of symptoms is reported by the patients.

INDEX: Triazolam, Benzodiazepines - Vestibular, Psychology - Human

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200

AUTHORS: Costa E., Silva, J.A., Acioli, A., Naylor, C., Jones, D.A., Silva, C., and Ferreira, I.

TITLE: Midazolam and Triazolam in Outpatients: A Double-blind Comparison of Hypnotic Efficacy

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, pp. 179S-183S, 1983.

DRUGS: Triazolam (TZ) 0.5 mg
Midazolam (MZ) 15 mg

SUBJECTS: Human - 198

PROCEDURE: The subjects received a drug for 2 consecutive nights and completed a questionnaire each day upon awakening.

FINDINGS: Both drugs significantly shortened the sleep-onset latency, reduced the number of awakenings, and increased the total sleep time. The patients' mental state upon awakening was significantly improved after both compounds for several self-rated items. The patients' feeling of being under drug influence was reported as being significantly more marked after TZ.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

210

AUTHORS: Dahl, L.E., Dencker, S.J., Lundin, L., and Kullingsjo, H.

TITLE: Comparison of Nitrazepam with Triazolam in Insomniac Outpatients

REFERENCE: Acta Psychiatrica Scandinavia, Vol. 65, pp. 86-92, 1982.

DRUGS: Triazolam (TZ) 0.5 mg
Nitrazepam (NZ) 5 mg

SUBJECTS: Human - 49

PROCEDURES: The effects of TZ were compared in a 7-day double-blind study with the longer acting NZ. Patients completed a sleep questionnaire.

FINDINGS: All significant differences favored the use of TZ. On the first night, TZ was significantly more effective than NZ in inducing and maintaining sleep and in increasing its overall duration. The patients' subjective preference, reflecting the depth of sleep experienced and the effect of the medication, reached highly significant levels in favor of TZ. Later in the study, the differences between the drugs disappeared, although the depth of sleep was better with TZ.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

220

AUTHORS: Danneberg, P. and Weber, K.H.

TITLE: Chemical Structure and Biological Activity of the Diazepines

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, pp. 231S-243S, 1983.

DRUGS: Diazepines

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: "The main pharmacological effects of the diazepines are exerted on emotional behavior, muscular tone and motor coordination.... The diazepines affect primarily the limbic system and only in higher doses inhibit the reticular vigilance and arousal system.... Binding sites were found and their highest density was in the central cortex, the cerebellum and the structures of the limbic system."

COMMENT: Excellent review article that examines many aspects of basic biochemistry.

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular, Vision, Acoustics, Chemistry - Human and Nonhuman

230

AUTHORS: Deacon, R.M.J. and Gardner, C.R.

TITLE: The Pull-up Test in Rats: A Simple Method for Evaluating Muscle Relaxation

REFERENCE: Journal of Pharmacological Methods, Vol. 11, pp. 119-124, 1984.

DRUGS: Benzodiazepines - doses vary
Barbiturates - doses vary
Antipsychotics - doses vary

SUBJECTS: Rats

PROCEDURES: The study used the pull-up test, which uses muscle lifting in inverted rats to measure muscle relaxation.

FINDINGS: Each of the benzodiazepines tested showed potent skeletal muscle relaxation effects. Some of the centrally acting drugs, such as meprobamate and barbiturates, demonstrated marked muscle relaxation effects, while the antipsychotics and morphine showed little effect. "We consider...the test has a useful place in the psychopharmacology laboratory."

INDEX: Triazolam, Benzodiazepines - Biomedical - Psychology - Nonhuman

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240

AUTHORS: Dehlin, O., Bjornson, G., Abrahamsson, L., and Smith, R.B.

TITLE: Pharmacokinetics of Triazolam in Geriatric Patients

REFERENCE: European Journal of Clinical Pharmacology, Vol. 25, pp. 91-94, 1983.

DRUGS: Triazolam 0.25 mg

SUBJECTS: Human - 8

PROCEDURES: Serum triazolam levels were obtained at hourly intervals in geriatric patients requiring daytime sedation. Oral administration was 1 h after breakfast for 7 consecutive days.

FINDINGS: No significant difference in serum concentrations between day 1 and day 7 were found. The average half-life of triazolam was about 1.5 h post administration.

INDEX: Triazolam, Benzodiazepines - Acoustics, Vision, Vestibular, Psychology, Chemistry - Human

250

AUTHORS: Dement, W., Seidel, W., and Carskadon, M.

TITLE: Issues in the Diagnosis and Treatment of Insomnia

REFERENCE: Psychopharmacology Supplement I, pp. 12-43, 1954.

DRUGS: Flurazepam
Triazolam

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: Chronic insomniacs demonstrated varying levels of daytime alertness but not significantly different from good sleepers. "The effect of flurazepam and triazolam on sleep improvement was essentially the same. . . .Triazolam improved not only nighttime sleep but also daytime alertness."

COMMENT: This lengthy article discusses insomnia of all types, and hypnotics and their use.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

260

AUTHORS: Dement, W., Seidel, W., and Carskadon, M.

TITLE: Daytime Alertness, Insomnia, and Benzodiazepines

REFERENCE: Sleep, Vol. 5, pp. S28-S45, 1982.

DRUGS: Review of several benzodiazepines (i.e., triazolam)

SUBJECTS: N/A

PROCEDURES: Reviews information from several studies and subject pools (i.e., insomniacs).

FINDINGS: Recently, two new trends have been used to evaluate hypnotic efficacy. First, the discovery of specific pathophysiological processes associated with insomnia has led to a diagnostic refinement, culminating in a formal and comprehensive nosology with over 60 specific diagnoses. Second, sleep cannot be considered apart from wakefulness, therefore treating insomnia is, or should be, a problem of the entire 24-h day.

COMMENT: If sleep can be clearly demonstrated to affect performance, then it may be a valid means of helping to better understand the performance effects of assigned drugs.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

270

AUTHORS: Dordain, G., Puech, A.J., and Simon, P.

TITLE: Triazolam Compared with Nitrazepam and with Oxazepam in Insomnia: Two Double-blind, Crossover Studies Analyzed Sequentially

REFERENCE: British Journal of Clinical Pharmacology, Vol. 11, pp. 43S-49S, 1981.

DRUGS: Triazolam (TZ) 0.50 mg
Nitrazepam (NT) 5 mg
Oxazepam (OZ) 50 mg

SUBJECTS: Human - Comparison of TZ and NZ: 54 patients (31 women and 23 men)
Comparison of TZ and OZ: 76 patients (59 women and 17 men)

PROCEDURES: Two double-blind, crossover studies comparing the hypnotic activity of TZ to NZ and OZ. The patients' preferences served as the main criterion and were processed by sequential analysis.

FINDINGS: Significantly more patients preferred TZ to NZ. The numbers of patients who preferred TZ to OZ did not differ significantly. Both TZ and OZ affected sleep parameters similarly except for onset of sleep and feeling in the morning, for which TZ seemed to be superior to OZ. Also, OZ produced significantly more side effects than did TZ (i.e., vertigo and difficulties upon awakening).

INDEX: Triazolam, Benzodiazepines - Vestibular, Psychology, - Human

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280

AUTHORS: Dorow, R.G., Seidler, J., and Schneider, H.H.

TITLE: A Radioreceptor Assay to Study the Affinity of Benzodiazepines and Their Receptor Binding Activity in Human Plasma Including Their Active Metabolites

REFERENCE: British Journal of Clinical Pharmacology, Vol. 13, pp. 561-565, 1982.

DRUGS: Lormetazepam (LM) 1 mg
Flunitrazepam (FM) 2 mg
Diazepam (V) 10 mg

SUBJECTS: Human - 8

FINDINGS: "Receptor affinities of numerous benzodiazepines (in vitro) show good correlation with therapeutic human doses."

COMMENT: A radioreceptor assay technique is used to detect small quantities of benzodiazepine.

INDEX: Triazolam, Benzodiazepines - Chemistry, Pharmacology - Human

AUTHORS: Drost, R.A.

TITLE: The Halcion Story

REFERENCE: Lancet, Vol. 1, No. 8176, pp. 1027-1028, 1980. (Letter to the editor).

DRUGS: Triazolam

SUBJECTS: N/A

PROCEDURES: N/A

FINDINGS: Drost takes exception with Lasagna's viewpoint (see Lancet, April 12) on events leading up to the suspension of the sales license for the hypnotic triazolam in the Netherlands in August 1979. Drost asserts that Lasagna did not attempt to collect and verify the facts.

COMMENT: A dispassionate and documented account of the actual events and related background is provided in Nederlandse Staatscourtant, Feb. 5 (No. 25, p. 3) and other recommended readings in the article.

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular, Vision - Human

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AUTHORS: Eberts, F.S., Philopoulos, Y., Reineke, L.M., and Vliek, R.W.

TITLE: Triazolam Disposition

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 29, No. 1, pp. 81-93, 1981.

DRUGS: Triazolam 0.88 mg

SUBJECTS: Human - 6

PROCEDURES: Normal adult males were given radiolabeled triazolam. Blood samples were drawn at intervals and assayed to measure absorption and clearance.

FINDINGS: "Triazolam was rapidly absorbed with a mean T1/2A. of 2.8 min." "Triazolam was rapidly eliminated with a mean T1/2E. of 2.3 hrs." "There was no accumulation of drug or active metabolite after repeated doses."

COMMENT: A well-constructed research design that avoids performance issues.

INDEX: Triazolam, Benzodiazepines - Chemistry - Human

310

AUTHORS: Einarson, T.R.

TITLE: Systematic Review of the Benzodiazepines

REFERENCE: British Medical Journal, Vol. 281, No. 6246, p. 1009, 1980.

DRUGS: Benzodiazepines

SUBJECTS: N/A

PROCEDURES: This is a comment on a previous article.

FINDINGS: Aggressive outburst and suicidal tendencies have only been reported with the longer-acting benzodiazepines.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

320

AUTHORS: Einarson, T.R. and Yoder, E.S.

TITLE: Triazolam Psychosis - A Syndrome?

REFERENCE: Drug Intelligence and Clinical Pharmacy, Vol. 16, No. 4, p. 330, 1982.

DRUGS: Triazolam 0.5 mg

SUBJECTS: Human - 1

PROCEDURES: Case report.

FINDINGS: A clinically depressed female on multiple drugs became disoriented and confused when given 0.5 mg triazolam. "Perhaps a triazolam syndrome does exist in susceptible individuals."

COMMENT: Mention is made of drug reaction versus idiopathic psychotic episode. Multiple drug therapy is mentioned as no problem.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

330

AUTHORS: Ellingsen, P.A.

TITLE: Double-blind Trial of Triazolam 0.5 mg vs. Nitrazepam 5 mg in Outpatients

REFERENCE: Acta Psychiatrica Scandinavia, Vol. 67, pp. 154-158, 1983.

DRUGS: Triazolam (TZ) 0.5 mg
Nitrazepam (NZ) 5 mg

SUBJECTS: Human - 40 patients (22 men and 18 women; mean age 42 years)

PROCEDURES: A double-blind crossover design was used on insomniac patients. The results were derived from a patient sleep questionnaire.

FINDINGS: Duration and latency of sleep and the number of awakenings during the night showed a significant difference in favor of TZ. An overall evaluation of sleep also showed TZ to be superior to NZ. Both drugs seemed to reduce dream activity and to alter the character of the dreams. Side effects did not differ significantly.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

340

AUTHORS: Fabre, L.F., Brachfeld, J., Meyer, L.R., Slowe, I.A., Calvo, R., and Metzler, C.

TITLE: Multi-clinic Double-blind Comparison of Triazolam and Placebo Administered for 14 Consecutive Nights in Outpatients with Insomnia

REFERENCE: The Journal of Clinical Psychiatry, Vol. 39, No. 8, pp. 679-82, 1978.

DRUGS: Triazolam 0.5 mg

SUBJECTS: Human - 239

PROCEDURES: One hundred and twenty-two patients with insomnia were given 0.5 mg triazolam for 14 days; 117 were given placebo. Each morning, questionnaires were completed to assess sleep onset, quality, duration, restfulness, and side effects.

FINDINGS: Ten patients on triazolam and 29 on placebo dropped-out because of "ineffectiveness" of the medication. Sixteen on triazolam and 16 on placebo dropped out due to side effects. "Triazolam was significantly better than placebo on all efficiency parameters measured. . . . Triazolam did not produce evidence of tolerance development after two weeks of treatment."

COMMENT: Large study of subjective data.

INDEX: Triazolam - Psychology - Human

350

AUTHORS: Fabre, L.F., Gainey, A., Kemple, S., McLendon, D.M., and Metzler, C.M.

TITLE: Pilot Open-label Study of Triazolam in the Treatment of Insomnia Following Alcohol Withdrawal

REFERENCE: Journal of Studies of Alcohol, Vol. 38, No. 11, pp. 2188-2192, 1977.

DRUGS: Triazolam 0.5-1.0 mg (dose adjustments allowed)

SUBJECTS: Human - 12 (alcoholics)

PROCEDURES: Sleep was subjectively assessed as depth of sleep, duration of sleep, and number of nightime awakenings. Assessment was made at 1, 2, and 4 weeks.

FINDINGS: Sleep was improved in all parameters examined. Results indicated reduced anxiety scores. Six patients were dropped from the study due to side effects.

INDEX: Triazolam, Alcohol - Psychology - Human

360

AUTHORS: Fabre, L.F., Gross, L., Pasigajen, V., and Metzler, C.

TITLE: Multiclinic Double-blind Comparison of Triazolam and Flurazepam for Seven Nights in Outpatients with Insomnia

REFERENCE: Journal of Clinical Pharmacology, Vol. 17, No. 7, pp. 402-409, 1977.

DRUGS: Triazolam 0.5 mg
Flurazepam 30 mg

SUBJECTS: Human - 110

PROCEDURES: Each patient was to keep a daily diary of sleep episodes at their own residences. Statistical analysis was made according to patient responses over a 7-d treatment period.

FINDINGS: Side effects that caused patients to be dropped from the study included five patients on triazolam (four serious side effects and one due to ineffectiveness) and three patients on flurazepam (one side effect and two because of ineffectiveness).

COMMENT: Subjective evaluations by patients.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

370

AUTHORS: Fabre, L.F., McLeudon, D.M., and Harris, R.T.

TITLE: Preference Studies of Triazolam with Standard Hypnotics in Outpatients with Insomnia

REFERENCE: Journal of International Medical Research, Vol. 4, pp. 247-254, 1976.

DRUGS: Triazolam (TM) 0.5 mg
Flurazepam (FM) 30 mg
Chloral Hydrate (CH) 500 mg

SUBJECTS: Human - 104 (insomniacs)

PROCEDURES: Insomniac patients involved in four different, 2-night double-blind crossover studies. A sleep questionnaire was used to assess onset, quality, and duration of sleep, as well as side effects.

FINDINGS: "The four studies indicated that outpatients suffering from insomnia preferred triazolam to FM or CH. . . . Triazolam was found to be better than flurazepam in sleep induction. . . . Triazolam was found better than CH in most parameters."

COMMENT: A purely subjective study.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

380

AUTHORS: Fabre, L.H. and Smith, W.T.

TITLE: Multi-clinic Crossover Comparison of Triazolam and Placebo in the Treatment of Coexisting Insomnia and Anxiety in Anxious Outpatients

REFERENCE: Diseases of the Nervous System, Vol. 38, No. 6, pp. 487-491, 1977.

DRUGS: Triazolam 0.25 mg

SUBJECTS: Human - 45

PROCEDURES: Double-blind crossover study of outpatients with insomnia and anxiety. Patient and physician evaluations were obtained. After 7 days, the medications were crossed-over with the placebo.

FINDINGS: Triazolam was significantly better than placebo in terms of onset of sleep, quality, duration, and restfulness. No differences in the evidence and quality of dreams were found. Triazolam was significantly superior to placebo in reducing anxiety as measured by the Target Symptoms Record, Hamilton Anxiety Rating Scale, and others.

INDEX: Triazolam - Psychology - Human

390

AUTHORS: File, S.E.

TITLE: Rapid Development of Tolerance to the Sedative Effects of Lorazepam and Triazolam in Rats

REFERENCE: Psychopharmacology, Vol. 73, pp. 240-245, 1981.

DRUGS: Lorazepam (LM) 0.25 and 0.5 mg/kg
Triazolam (TM) 0.075-0.25 mg/kg

SUBJECTS: Rats

PROCEDURES: Rats placed in a holeboard were monitored for head-dipping activity by photoelectric cells as a measure of exploration activity.

FINDINGS: Tolerance to the sedative effects of both drugs occurred after 3 days of pretreatment. "Development of tolerance did not require the continuous presence of drug in brain and plasma." Triazolam was faster acting than LM. "Changes in drug metabolism can account for some, but possibly not all, of the behavioral tolerance."

INDEX: Triazolam, Benzodiazepines - Psychology - Nonhuman

400

AUTHORS: Fontaine, R. and Bradwejn, J. (the article) Hendler, N. and Long, D. (the reply)

TITLE: The Effects of Benzodiazepines (A reply is also contained.)

REFERENCE: American Journal of Psychiatry, Vol. 138, No. 4, pp. 536-537, 1981.

DRUGS: Benzodiazepines

SUBJECTS: N/A

PROCEDURE: N/A

FINDINGS: The article mentions that other researchers seem confident about the use of the Weschler Adult Intelligence Scale (WAIS), the Bender-Gestalt, and the EEG to measure cognitive and psychomotor performance impairment caused by medication. The authors feel that these tests are perhaps too global and that research has identified more sensitive measures: threshold for critical flicker fusion, letter cancellation, and digit symbol substitution. THE RESPONSE: Hendler and Long agree that the use of the EEG, WAIS, and Bender-Gestalt tests are global and nonspecific, but this nonspecific effect occurred nearly twice as often in the group of patients taking just benzodiazepines than in the group just taking narcotics.

INDEX: Triazolam, Benzodiazepines - Psychology, Vision-Human

410

AUTHORS: Freedman, D.X. (Chairman)

TITLE: Drugs and Insomnia: The Use of Medication to Promote Sleep

REFERENCE: Consensus Development Conference Statement, 15-17 November 1983 (a draft).

DRUGS: Benzodiazepines

SUBJECTS: N/A

PROCEDURES: Treatment strategies for insomnia are discussed.

FINDINGS: Unlike many other benzodiazepines, triazolam has no active metabolite. Even though triazolam has little or no cumulative effects, due to its short half-life (3-4 h), there is still unwanted tolerance. Although the benzodiazepines in therapeutic doses generally do not appear to inhibit or enhance the metabolism of other drugs, their effects do interact with ethanol and other sedative hypnotics. Thus, the central nervous system depressant effects of alcohol and the other benzodiazepines are additive.

INDEX: Triazolam, Alcohol - Psychology - Human

420

AUTHORS: Gall, M., Kamdar, B., and Collins, R.J.

TITLE: Pharmacology of Some Metabolites of Triazolam, Alprazolam, and Diazepam Prepared by a Simple, One-step Oxidation of Benzodiazepines

REFERENCE: Journal of Medical Chemistry, Vol. 21, No. 12, pp. 1290-1294, 1978.

DRUGS: Triazolam

SUBJECTS: Nonhuman

PROCEDURES: Triazolam and two principle metabolites (alpha, 4-dihydroxy triazolam, and alphahydroxy triazolam) were tested for pharmacological activity.

FINDINGS: The dihydroxy metabolite had very little pharmacologic activity. The one alpha hydroxy metabolite has considerable biologic activity as the parent compound (triazolam); but, because serum concentrations are so low with this metabolite, it probably contributes very little to the action of triazolam. Neither metabolite accumulates in tissues.

INDEX: Triazolam, Benzodiazepines - Chemistry - Nonhuman

430

AUTHORS: Goetzke, E., Findeisen, P., and Welbers, I.B.

TITLE: Comparative Study on the Efficacy of and the Tolerance to the Triazolodiazepines, Triazolam and Brotizolam

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, No. 2, pp. 407S-412S, 1983.

DRUGS: Triazolam (TZ) 0.25 mg
Brotizolam (BZ) 0.25 mg

SUBJECTS: Human - 86

PROCEDURES: A double-blind crossover trial was used, and the ingestion of drugs was randomized. The duration of the study was 14 d, and each assessment period lasted 7 d. Each morning, the patients evaluated their sleep and early morning alertness.

FINDINGS: Over a 6-d period, efficacy and tolerance did not differ. The physicians reported the effectiveness of the drugs to be good-to-satisfactory in 88.6% of the subjects with BZ and 92.0% with TZ. The patients reported (with both drugs) reduced time to fall asleep, less awakenings, increased duration of sleep, and improved condition on awakening. Side effects were reported by five patients (two with BZ and three with TZ), involving hangover and mild skin allergy.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

440

AUTHORS: Gorenstein, C. and Gentil, V.

TITLE: Residual and Acute Effects of Flurazepam and Triazolam in Normal Subjects

REFERENCE: Psychopharmacology, Vol. 80, pp. 375-379, 1983.

DRUGS: Flurazepam (FZ) 15 and 30 mg
Triazolam (TZ) 0.25 and 0.5 mg

SUBJECTS: Human - 6

PROCEDURES: Treatment intervals were 1 week apart. Physiological measures were blood pressure, pulse rate, pupil size, and critical flicker-fusion threshold (CFF). Psychological tests included the Digit Symbol Substitution Test (DSST), the Symbol Copying Test (SCT), a cancellation task (CT), and the Ball Bearing Test. The following rating scales were used: a modified visual analogue mood scale (VAMS-m), a modified body symptom scale (BSS-m), an eight-item visual analogue global impression scale (GIS), and a six-item visual analogue experimenter observation scale (EOS). Lastly, the procedure included a modified sleep evaluation questionnaire (SEQ-m).

FINDINGS: Doses of both drugs produced hangover effects, impairing motor performance and increasing sleepiness the following morning. The effects of FZ were mild and hard to distinguish from those of the placebo.

INDEX: Triazolam, Benzodiazepines - Vision, Psychology - Human

AUTHORS: Gram, L.F.

TITLE: The Contribution of Pharmacokinetics to the Best Use of Benzodiazepines and Antidepressants

REFERENCE: L'Encephale, Vol. 8, pp. 291-298, 1982.

DRUGS: Benzodiazepines
Antidepressants

SUBJECTS: N/A

PROCEDURES: Review article regarding basic pharmacology and the differences between the two classes of drugs.

FINDINGS: "A major significance of pharmacokinetics of antidepressants thus is, that therapy guided by monitoring of plasma levels of active compounds will improve both safety and efficacy of the treatment."

INDEX: Triazolam, Benzodiazepines - Psychology - Human

AUTHORS: Greenblatt, D.J., Divoll, M., Abernathy, D.R., and Shader, R.I.

TITLE: Benzodiazopine Hypnotics: Kinetic and Therapeutic Options

REFERENCE: Sleep, Vol. 5, pp. 518-527, 1982.

DRUGS: Benzodiazopines

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: The paper reviews seven compounds, as well as their derivatives, comparing rates of absorption and elimination. Temazepam uptake and elimination rates are slow, suggesting possible residual, cumulative effects.

INDEX: Triazolam, Benzodiazepines - Acoustics, Vestibular, Vision, Biomedical, Psychology - Human

470

AUTHORS: Greenblatt, D.J., Shader, R.I., Dovall, M., and Harmatz, J.S.

TITLE: Adverse Reactions to Triazolam, Flurazepam, and Placebo in Controlled Clinical Trials

REFERENCE: Journal of Clinical Psychiatry, Vol. 45, No. 5, pp. 192-195, 1984.

DRUGS: Triazolam (TZ) 0.25-0.50 mg
Flurazepam (FZ) 30 mg

SUBJECTS: Human - (TZ 0.25 mg, n = 731) (TZ 0.5 mg, n = 2004)
(FZ n = 899)

PROCEDURES: Clinical trials (45 double-blind)
Usually without washout between trials
Interview and self rating.

FINDINGS: Complaints associated with FZ were drowsiness, dizziness, fatigue, or incoordination (CNS). Triazolam was intermediate to placebo and FZ. All other adverse reactions equal or more frequent with placebo.

COMMENT: No normal controls were used, and all subjects were patients. Self reports.

INDEX: Triazolam, Benzodiazepines - Vestibular, Biomedical - Human

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480

AUTHORS: Griffiths, R.R., Lamb, R.J., Ator, N.A., Roache, J.D., and Brady, J.V.

TITLE: Relative Abuse Liability of Triazolam: Experimental Assessment in Animals and Humans

REFERENCE: Neuroscience and Behavioral Review, Vol. 9, pp. 133-151, 1985.

DRUGS: Triazolam
Benzodiazepines
Barbiturates

SUBJECTS: N/A

PROCEDURES: Review of 168 articles.

FINDINGS: "Triazolam has relatively less abuse potential than the intermediate barbiturates such as pentobarbital." We have no clear indication that triazolam has greater abuse potential than other benzodiazepines. Speculation exists that triazolam has greater toxicity than other benzodiazepines, and data suggest that triazolam may have a greater amnestic effect than pentobarbital.

INDEX: Triazolam, Benzodiazepines - Psychology - Human, Nonhuman

AUTHORS: Gudgeon, A.C. and Hindmarch, I.

TITLE: Midazolam: Effects on Psychomotor Performance and Subjective Aspects of Sleep and Sedation in Normal Volunteers

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, pp. 121S-126S, 1983.

DRUGS: Midazolam 5, 10, 15, and 20 mg

SUBJECTS: Human - 12

PROCEDURES: Twelve normal volunteers were employed in two experiments using Choice Reaction Time (CRT), Critical Flicker Fusion Frequency (CFFF), and Leeds Sleep Evaluation Questionnaire (LSEQ). Four doses and matching placebos were used.

FINDINGS: The CRT test showed a dose-related, progressive impairment of task performance. A significant decrement in CFFF thresholds was found with Midazolam at all doses. Subjects rated the drugs similarly, reflecting the CRT and CFFF findings.

COMMENT: Midazolam has significant sedative effects, which were not observed at 7 or 12 h post-administration.

INDEX: Benzodiazepines - Psychology, Vision - Human

AUTHORS: Gurwich, E., Cohon, M., Olree J., Cramer, R., and Pugsley, J.

TITLE: Halcion (Triazolam): Pharmacokinetic Profile

REFERENCE: Upjohn Company Tech Report, Feb., 1985. Drug Information Services Unit (9182).

DRUGS: Triazolam

SUBJECTS: Human and nonhuman

PROCEDURE: A review of published and unpublished data on triazolam through September 1984.

FINDINGS: (1) Triazolam is soluble in chloroform and insoluble in water; (2) the pKa = 1.71; (3) administration of 0.5 mg TZ with food delayed absorption rate but not peak levels; (4) TZ is bound (89%) to serum albumin; (5) TZ elimination half-life = 1.8-4.6 h; (6) TZ is metabolized to six compounds, principally hydroxy derivatives with an average elimination half-life of 3.8 h; (7) the elimination of TZ in geriatric patients is reduced.

INDEX: Triazolam - Chemistry, Pharmacology - Nonhuman, Human

510

AUTHORS: Hendler, N., Cimini, C., Terence, M.A., and Long, D.

TITLE: A Comparison of Cognitive Impairment Due to Benzodiazepines and to Narcotics

REFERENCE: American Journal of Psychiatry, Vol. 137, pp. 828-830, 1980.

DRUGS: Benzodiazepines (BZ) and narcotics. (The patients were screened for the drug; amounts are not clearly reported.)

SUBJECTS: Human - 106 patients admitted during a 6-month period; 64 (60%) were taking BZ; 21 were taking narcotics alone, and 18 were taking BZ alone.

PROCEDURES: Thirteen of the 18 BZ patients had an EEG, as well as the full battery of psychological tests (Weschler Adult Intelligence Scale, Memory Quotient, and Bender-Gestalt); 13 of the 21 patients taking narcotics alone also completed the same tests.

FINDINGS: Patients receiving narcotics alone and a group of patients not receiving medication did not show signs of cognitive impairment. The effects of BZ on sleep and perception of chronic pain, in combination with the cortical changes that they produce, imply that these drugs should not be used in most patients with chronic pain.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

520

AUTHORS: Hill, S.Y., Goodwin, D.W., Reichman, J.B., Mendelson, W.B., and Hopper, S.

TITLE: A Comparison of Two Benzodiazepine Hypnotics Administered with Alcohol

REFERENCE: Journal of Clinical Psychiatry, Vol. 43, pp. 408-410, 1982.

DRUGS: Triazolam (TM) 0.25 and 0.5 mg
Flurazepam (FM) 30 mg
Alcohol 0.8g/kg body wt

SUBJECTS: Human - 56

PROCEDURES: Drugs were administered to healthy volunteers in a double-blind manner with combinations of alcohol- placebo or alcohol-drug. The pursuit rotor test (PRT), attention test (AT), Romberg test (RT), tweezer dexterity test (TDT), word association test (WAT), digit symbol (DS), and digit span (DS) were administered.

FINDINGS: Larger doses of TM with alcohol produced adverse symptoms in all subjects and were discontinued. Additive effects were found in only two tests, the RT and the WAT. Alcohol and TM together produced an additive impairment of balance.

INDEX: Triazolam, Benzodiazepines, Alcohol - Psychology, Vestibular, Vision - Human

530

AUTHORS: Hindmarch, I. and Clyde, C.A.

TITLE: The Effects of Triazolam and Nitrazepam on Sleep Quality, Morning Vigilance and Psychomotor Performance

REFERENCE: Arzneimittel-Forschung Drug Research, Vol. 30, No. 7, pp. 1163-1166, 1980.

DRUGS: Triazolam (TM) 0.5 mg
Nitrazepam (NM) 10 mg

SUBJECTS: Human - 20

PROCEDURES: Reaction time, critical flicker fusion (CFF) threshold, and mental arithmetic ability were measured on the morning following bedtime administration of the drug.

FINDINGS: "Both drugs were rated as effective hypnotics." Early morning performance impairment was found with NM but not TM. Following initial doses of NM, CFF thresholds were depressed but increased following TM.

COMMENT: The residual sedative effects were greater with NM.

INDEX: Benzodiazepines, Triazolam - Vision, Psychology - Human

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540

AUTHORS: Jochemsen, R., Wesselman, J.G., van Boxtel, C.J., Hermans, J., and Breimer, D.D.

TITLE: Comparative Pharmacokinetics of Brotizolam and Triazolam in Healthy Subjects

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, 291S-297S, 1983.

DRUGS: Triazolam 0.5 mg
Brotizolam 0.5 mg

SUBJECTS: Human - 8

PROCEDURES: A crossover design was used with oral administration and venous sampling up to 24 h (Triazolam) and 48 h (Brotizolam).

FINDINGS: Peak times for plasma drug level were 1.1 + 1.0 h for brotizolam and 1.2 + 0.5 h for triazolam. Elimination half-life was 2 times greater in brotizolam (5.0 + 1.1 h vs 2.6 $\pm$ 0.7 h). Uptake kinetics varied in some subjects for TZ.

INDEX: Triazolam, Benzodiazepines - Chemistry, Pharmacology - Human

550

AUTHORS: Johnson, L.C. and Chernik, D.A.

TITLE: Sedative-hypnotics and Human Performance

REFERENCE: Psychopharmacology, Vol. 76, pp. 101-113, 1982.

DRUGS: Eight different benzodiazepines and five different barbiturates

SUBJECTS: N/A

PROCEDURES: A review article of 52 separate studies with emphasis on psychomotor performance.

FINDINGS: Drug-related daytime performance did not improve. Long-acting drugs generally showed more performance decrement than short-acting drugs. Sedative-hypnotics generally improved the quality of sleep but not the daytime performance.

COMMENT: A comprehensive review of the literature comparing available sedative-hypnotics.

INDEX: Benzodiazepines, Triazolam - Psychology - Human

560

AUTHORS: Johnson, L.C., Mitler, M.M., and Dement, W.C.

TITLE: Comparative Hypnotic Effects of Flurazepam, Triazolam, and Placebo: A Reanalysis

REFERENCE: Naval Health Research Center, 1984, Report No. 84-13.

DRUGS: Flurazepam (FZ) 30 mg
Triazolam (TZ) 0.5 mg
Placebo

SUBJECTS: Human - 32

PROCEDURES: Chronic insomniacs were studied for 59 nights in a parallel group design.

FINDINGS: (1) "Placebo had no consistent impact on any sleep variables."
(2) TZ patients displayed marked sleep latency increases in the first 2 withdrawal nights but no rebound in awake time after sleep onset.
(3) FZ latency-to-sleep onset occurred over a much longer period than TZ.

COMMENT: Short-acting benzodiazepines appear to prevent rebound wakefulness after sleep onset better than long-acting BZ. Withdrawal sleep latency appears confined to 1 or 2 nights with TZ, and may be irregular up to 2 weeks with FZ.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

570

AUTHORS: Johnson, L.C. and Spinweber, C.L.

TITLE: Effects of a Short-acting Benzodiazepine on Brain Electrical Activity During Sleep

REFERENCE: Naval Health Research Center, 1981, Report No. 81-2.

DRUGS: Triazolam 0.5 mg

SUBJECTS: Human - (12 insomniacs)

PROCEDURES: Days 1 through 3 were placebo days, days 4 through 10 were either placebo or drug days, and days 11 through 12 were placebo days. The EEG auditory-evoked responses were recorded, and on the sixth night, patients were tested at 1.5, 3, 5, and 7.5 h for cognitive and visual motor performance tasks.

FINDINGS: (1) TZ decreased latency-to-sleep onset and increased the duration of sleep.
(2) TZ caused no rebound insomnia as analyzed by EEG (delta waves, spindle count). In other words, EEG returned to baseline after TZ patients stopped taking the drug.
(3) Some performance cognitive tests were affected at 1.5, 3, and 5 h, but not at 7.5 h.

INDEX: Triazolam - Acoustics, Vision, Psychology - Human

580

AUTHORS: Johnson, L.C. and Spinweber, C.L.

TITLE: Benzodiazepine Effects on Arousal Threshold During Sleep

REFERENCE: Naval Health Research Center, 1983, Report 83-17.

DRUGS: Flurazepam 30 mg
Triazolam 0.5 mg

SUBJECTS: Human - 32

PROCEDURES: "Poor sleepers" in each group were given placebo for 6 or 7 nights, followed by the drug under consideration for 10 nights, followed by placebo for several withdrawal nights. Arousal thresholds were measured.

FINDINGS: Both drugs increased arousal threshold, particularly in the earlier periods of sleep. Benzodiazepines may not be of great use for inducing sleep in a noisy environment, but once sleep is well established, arousal by noise is more difficult.

COMMENT: Build up of long-acting drug metabolites does not appear to change thresholds for arousal.

INDEX: Benzodiazepines, Triazolam - Acoustics - Human

590

AUTHORS: Johnson, L.C., Spinweber, C.L., Seidel, W.F., and Dement, W.C.

TITLE: Sleep Spindle and Delta Changes During Chronic Use of a Short-acting and a Long-acting Benzodiazepine Hypnotic

REFERENCE: Electroencephalography and Clinical Neurophysiology, Vol. 55, pp. 662-667, 1983.

DRUGS: Triazolam 0.5 mg
Flurazepam 30 mg

SUBJECTS: Human - 21

PROCEDURES: Diagnosed insomniacs were given 3 nights adaptation rest and 9 placebo nights. For the next 37 nights, 7 subjects each received placebo, flurazepam, or triazolam, followed by a 10-night placebo withdrawal period. All-night EEGs were recorded. Plasma analyses were recorded.

FINDINGS: Plasma levels accumulated with flurazepam but were undetectable with triazolam. By the sixth night, EEG spindle rates with both drugs increased. Upon withdrawal of the drug, both groups showed gradual return of the spindle rate to baseline. In both groups, EEG delta activity was decreased, but only late in the study. Both groups returned to baseline within 4 to 10 d.

COMMENT: This conflicts with other studies by the same authors (1981) where spindle rates returned to baseline immediately following withdrawal of triazolam.

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular - Human

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600

AUTHORS: Juhl, R.P., Daugherty, V.M., and Kroboth, P.D.

TITLE: Incidence of Next-day Anterograde Amnesia Caused by Flurazepam Hydrochloride and Triazolam

REFERENCE: Clinical Pharmacy, Vol. 3, pp. 622-625, 1984.

DRUGS: Triazolam 0.125-0.50 mg
Flurazepam 15-30 mg

SUBJECTS: Human - 54 (in hospital for at least 3 months)

PROCEDURES: Hospital-bed interviews with recall items. Stanford Sleepiness Scale used along with medical histories; administered at 8 a.m. with retest at 11 a.m.

FINDINGS: No memory impairment was reported with the use of triazolam (same as control). Significant memory impairment was noted with flurazepam. The amnestic effects seem to be related to patient drowsiness.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

610

AUTHORS: Kales, A. and Kales, J.D.

TITLE: Sleep Laboratory Studies of Hypnotic Drugs: Efficacy and Withdrawal Effects

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 3, No. 2, pp. 140-150, 1983.

DRUGS: Flurazepam (FZ) 30 mg
Triazolam (TZ) 0.5 mg
Temazepam (TZP) 30 mg

SUBJECTS: Human - (insomnia patients)

PROCEDURES: Sleep studies.

FINDINGS: Although sleep was markedly improved on the first night of FZ administration, peak effectiveness did not occur until the second or third night. These data suggest that the short elimination half-life components of the drug contribute in a major way to both the drug's sleep induction and sleep-maintenance-promoting properties. With short-time TZ use, both sleep induction and sleep maintenance improved, with total awake time decreasing (45% from baseline) markedly. At the end of 2 weeks of drug use, none of the efficacy parameters were significantly increased above baseline levels, possibly indicating tolerance or rebound insomnia. Further, following drug withdrawal, sleep difficulty significantly increased above baseline levels. Similar conditions were produced with TZP.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

620

AUTHORS: Kales, A., Scharf, M.B., Kales, J.D., and Soldatos, C.R.

TITLE: Rebound Insomnia: A Potential Hazard Following Withdrawal of Certain Benzodiazepines

REFERENCE: Journal of the American Medical Association, Vol. 241, No. 16, pp. 1692-1695, 1979.

DRUGS: Triazolam (TZ) 0.5 mg, Nitrazepam (NZ) 0.5 and 10 mg, Flunitrazepam (FZ) 1 and 2 mg, Flurazepam (FZP) 30 mg, Diazepam (V) 5-20 mg

SUBJECTS: Human

PROCEDURES: Subjects were monitored by EEG and EOG. All EEG records were scored visually.

FINDINGS: Rebound insomnia, a worsening of sleep compared with baseline, occurred following withdrawal of TZ, NZ, and FZ after single nightly doses for short periods. The rebound insomnia was attributed to the short and intermediate half-lives of these drugs. Drugs V and FZP, which have longer half lives, did not cause rebound insomnia on withdrawal. Rebound insomnia may play a role in the development of hypnotic drug dependence with shorter-acting benzodiazepine drugs.

INDEX: Triazolam, Benzodiazepines - Vision, Psychology - Human

630

AUTHORS: Kales, A., Soldatos, C.R., Bixler, E.O., and Kales, J.D.

TITLE: Early Morning Insomnia with Rapidly Eliminated Benzodiazepines

REFERENCE: Science, Vol. 220, pp. 95-97, 1983.

DRUGS: Midazolam (MZ) 20 mg
Triazolam (TZ) 0.5 mg
Flurazepam (FZP) 30 mg
Quazepam (QZP) 30 mg

SUBJECTS: Human (insomniacs)

PROCEDURES: Monitoring by hypnopolygraphic recordings of an EEG, EMG, and EOG.

FINDINGS: All four drugs decreased the time spent awake during the first 6 h of the night on each of the two sets of three consecutive drug nights. This effect was variable across drugs for the last 2 h of the night. Drugs MZ and TZ were less effective at decreasing mean awake time during the last 2 h of sleep than the longer acting FZP and QZP compounds.

COMMENT: Because the vast majority of REM sleep occurs during the last 2 h of sleep, the above findings may be of considerable physiologic and performance concern.

INDEX: Triazolam, Benzodiazepines - Psychology, Vision - Human

640

AUTHORS: Kamp, C.W. and Morgan, W.W.

TITLE: Benzodiazepines Suppress the Light Response of Retinal Dopaminergic Neurons in Vivo

REFERENCE: European Journal of Pharmacology, Vol. 77, pp. 343-346, 1982.

DRUGS: Diazepam 76 mol/kg i.p.
Flurazepam 0.5 or 1.0 mol/eyeball

SUBJECTS: Rats - 32

PROCEDURES: All rats were dark adapted: 16 were controls, and 16 were injected with diazepam. Thirty minutes later, half of each group was given a tyrosine hydroxyphase inhibitor, exposed to room light for 1 h, and sacrificed. Retinas were removed and frozen. Dopamine was then assayed.

FINDINGS: (1) Results were consistent with a diazepam-mediated suppression of dopamine turnover.
(2) Results were consistent with a flurazepam-mediated inhibition of light-enhanced dopamine synthesis.

COMMENT: Findings may be relevant to visual-effects testing.

INDEX: Benzodiazepines - Vision - Nonhuman

650

AUTHORS: Keighley, M.R.B., Gannon, M., Warlow, J., Jenkins, C.R.M., and Gammon, R.J.

TITLE: Evaluation of Single-dose Hypnotic Treatment Before Elective Operation

REFERENCE: British Medical Journal, Vol. 281, pp. 829-831, 1980.

DRUGS: Triazolam (TZ) 0.25 mg
Flurazepam (FZP) 15 mg

SUBJECTS: Human - 96 (pre-op patients)

PROCEDURES: Patient questionnaire; a prospective, randomized, double-blind, controlled trial.

FINDINGS: The onset of sleep was delayed, and the duration of sleep was reduced in two-thirds of the patients taking the placebo compared with their normal sleep pattern. Both drugs significantly improved the duration and time of onset of sleep and reduced the frequency of awakenings when compared with the placebo. Patients who received TZ, however, fell asleep faster and woke less often than those receiving FZP. Furthermore, TZ patients appeared to have advantages over FZP patients before major surgery. The study promotes TZ as being safe and effective for use before major surgery.

INDEX: Triazolam, Benzodiazepines - Psychology, - Human

660

AUTHORS: Kroboth, P.D. and Juhl, R.P.

TITLE: Triazolam (Halcion, The Upjohn Company)

REFERENCE: Drug Intelligence and Clinical Pharmacy, Vol. 17, pp. 495-500, 1983.

DRUGS: Triazolam (TZ) 0.125-0.5 mg

SUBJECTS: N/A

PROCEDURES: Drug review or evaluation.

FINDINGS: The review discusses pharmacology, pharmacokinetics (absorption, distribution, metabolism, elimination, and serum concentrations), clinical studies (objective sleep evaluations, daytime psychomotor performance testing, as well as subjective evaluations and patient preferences, residual effects, and geriatric patients), toxicity, side effects and adverse reactions, drug interactions, dosage and administration, availability, and cost. The article presents a brief drug summary.

COMMENT: Most of the above information is not contained verbatim directly in the article, however, references are listed for the reader. It is an excellent overall review of the drug.

INDEX: Triazolam - Chemistry, Psychology - Human

670

AUTHORS: Kudo, Y.

TITLE: Hypnotic Effects of a Benzodiazepine Derivative: A Clinical Observation

REFERENCE: International Pharmacopsychiatry, Vol. 17, pp. 49-64, 1982.

DRUGS: Triazolam (TZ) 0.5 mg
Nitrazepam (NZP) 5 mg

SUBJECTS: Patients (N = 268) diagnosed with psychoneurosis, depression, or schizophrenia, or borderline cases who complained of insomnia.

PROCEDURES: The following procedures were used: Global improvement rating (GIR), preference of the two drugs on a five-point scale by doctor and patient, and rating of side effects on a four-point scale. Evaluation of the laboratory findings and evaluation of the level of dependency were made by the doctor alone.

FINDINGS: Statistically significant differences were demonstrated in favor of TZ compared with NZP in many aspects of efficacy, but were not significantly different between TZ and NZP in the incidence of concomitant symptoms and side effects. The fact that a certain quantity of TZ is equivalent in strength to 10 times that quantity of NZP suggests the high potency of the former. These data indicate that TZ is a valuable sleep inducer, with highly rated efficacy and safety.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

680

AUTHORS: Kusaka, M., Horikawa, A., Meshi, T., and Maruyama, Y.

TITLE: Interaction of Triazolam with Desipramine

REFERENCE: Psychopharmacology, Vol. 70, pp. 255-261, 1980.

DRUGS: Triazolam (TM) 1 mg/kg, i.p.
Desipramine (DM) 10 mg/kg, i.p.
Pentobarbital

SUBJECTS: Rats - 24

PROCEDURES: Laboratory rats were injected with the listed drugs in both single and repeated doses to determine brain catecholamine levels, sleeping times, and muscle relaxation.

FINDINGS: "TM and DM given alone and in combination were synergistic with pentobarbital hypnosis."
"Repeated treatment with DM alone repressed body weight gain."
"TM induced muscle relaxation acutely, but was not affected by concomitant DM treatment."
"TM and DM given in combination produced hypothermia,...but given separately did not."

COMMENT: Norepinephrine levels decreased when drugs were used in combination. Single drug effects are unclear.

INDEX: Triazolam - Nonhuman

690

AUTHORS: Ladimer, I.

TITLE: Trials and Tribulations of Triazolam - A Commentary

REFERENCE: Journal of Clinical Pharmacology, Vol. 20, No. 2-3, pp. 159-161, 1980.

DRUGS: Triazolam

SUBJECTS: N/A

PROCEDURES: An editorial.

FINDINGS: Triazolam appeared to be a useful and safe hypnotic until the observations of a Dutch psychiatrist, Dr. Loss Van der Kroef, appeared in an unrefereed publication. Van der Kroef described unusual adverse effects on eight of his patients. These effects ranged from no hypnotic effects to paranoia to hallucinations. This editorial questions the reliability of these findings, as disclosure of patient facts and interpretations were not given.

COMMENT: An avid Dutch press may be partially responsible for the removal of triazolam from their market.

INDEX: Triazolam - Vision, Acoustics, Vestibular, Psychology - Human

700

AUTHORS: Lasagna, L.

TITLE: The Halcion Story: Trial by Media

REFERENCE: Lancet, Vol. 1, No. 8172, pp. 815-816, 1980 (point of view): Lancet, Vol. 1, No. 8181, pp. 1304-1305, 1980 (letter to the editor).

DRUGS: Triazolam (TZ) (Halcion)

SUBJECTS: N/A

PROCEDURES: Comment on the pharmaco-politico effects of flamboyant media coverage.

FINDINGS: Triazolam "has been alleged to produce unique and serious adverse side effects on the central nervous system. In the Netherlands, television and newspaper coverage of reported side effects were followed by a temporary suspension of the drug there. The reported adverse reactions resemble those known to occur occasionally after use of older benzodiazepines and other central nervous system drugs. Whatever the final verdict on triazolam may be, there is reason to question whether regulatory decisions forced by flamboyant media coverage are in the public interest."

INDEX: Triazolam - Psychology - Human

710

AUTHORS: Lingjaerde, O. and Bratlid, T.

TITLE: Triazolam (Halcion) Versus Flunitrazepam (Rohyphol) Against Midwinter Insomnia in Northern Norway

REFERENCE: Acta Psychiatrica Scandinavica, Vol. 64, pp. 260-269, 1981.

DRUGS: Triazolam (TZ) 0.25 mg
Flunitrazepam (FZP) 1 mg

SUBJECTS: Human - 19

PROCEDURES: A double-blind crossover trial was used. Each drug was given for 5 nights in random order. Recorded sleep variables were sleep latency, number of awakenings, duration of sleep, quality of sleep, and feeling in the morning. These were quantified to provide an overall sleep evaluation score.

FINDINGS: No differences were found between TZ or FZP on any single variable. In addition, eight patients stated a preference for TZ and eight for FZP. Only three patients complained about side effects. Notably, the feeling of being alert and refreshed in the morning was significantly superior during active drug (TZ and FZP) periods as compared to the placebo periods.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

720

AUTHORS: Lipani, J.A.

TITLE: Preference Study of the Hypnotic Efficacy of Triazolam 0.125 mg Compared to Placebo in Geriatric Patients with Insomnia

REFERENCE: Current Therapeutic Research, Vol. 24, No. 4, pp. 397-402, 1978.

DRUGS: Triazolam 0.125 mg

SUBJECTS: Human - 42

PROCEDURES: A 2-night, double-blind crossover study of geriatric insomniacs was carried out. Subjects were questioned on triazolam efficacy and side effects.

FINDINGS: Triazolam was significantly better than the placebo in helping promote sleep, reducing latency, and improving morning alertness. Side effects reported were drowsiness, dizziness, headache, and stomach ache.

COMMENT: One of many subjective studies of sleep latency, quality, and duration.

INDEX: Triazolam - Psychology - Human

730

AUTHORS: MacLeod, N.

TITLE: Triazolam: Monitored Release in the United Kingdom

REFERENCE: British Journal of Clinical Pharmacology, Vol. 13, pp. 51S-53S, 1981.

DRUGS: Triazolam (TZ) 0.125-0.5 mg

SUBJECTS: Human - 3010

PROCEDURES: A monitored release for TZ was carried out in the U.K. during 1979. Each practitioner was provided with a questionnaire with yes and no response blanks.

FINDINGS: The majority of patients (71.3%) took 0.25 mg TZ, 24.1% took 0.125 mg, and only 4.4% took 0.5 mg TZ. The majority of patients (84.7%) reported an adequate night's sleep, and the overall incidence of side effects in patients taking the drug was 12.2%. Side effects most frequently reported were related to the central nervous system such as drowsiness, headache, dizziness, restlessness, tiredness, impaired coordination, giddiness, and some nightmares.

INDEX: Triazolam - Vestibular, Psychology - Human

740

AUTHORS: MacLeod, N. and Kratochvil, C.H.

TITLE: Behavioral Reactions to Triazolam

REFERENCE: Lancet, Vol. 2, No. 8143, pp. 638-639, 1978 (letter to the editor).

DRUGS: Triazolam (TZ)

SUBJECTS: N/A

PROCEDURES: N/A

FINDINGS: The behavioral side effects reported by Dr. van der Kroef (Sept. 8, p. 526) are contrary to the vast majority of data collected at that time. More than 8000 patients have received TZ in clinical trials throughout the world, which shows that TZ produces a lower incidence of such side effects as depression, confusion, nightmares, and concentration difficulties than does flurazepam.

INDEX: Triazolam - Psychology - Human

750

AUTHORS: Mamelak, M., Csima, A., and Price, V.

TITLE: A Comparative 25-night Sleep Laboratory Study on the Effects of Quazepam and Triazolam on Chronic Insomnia

REFERENCE: Journal of Clinical Pharmacology, Vol. 24, pp. 65-75, 1984.

DRUGS: Triazolam 0.5 mg
Quazepam 30 mg

SUBJECTS: Human - 12 (insomniacs)

PROCEDURES: Drugs were administered double-blind; EEG sleep recordings were made and scored blind. The subjects were studied for 25 consecutive nights (15 nights in sleep lab). Recordings included baseline, early drug, intermediate drug, and early and late withdrawal.

FINDINGS: Both drugs were effective in improving sleep (objective and subjective). Triazolam increased REM latency but increased REM sleep during withdrawal. The article reports possible insomnia on the first day of withdrawal.

COMMENT: The chronic post-withdrawal insomnic effects of triazolam or quazepam were not supported.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

760

AUTHORS: Mattila, M.J.

TITLE: Interactions of Benzodiazepines on Psychomotor Skills

REFERENCE: British Journal of Clinical Pharmacology, Vol. 18, pp. 21S-26S, 1984.

DRUGS: Benzodiazepines (BZ)

SUBJECTS: N/A

PROCEDURES: Review article

FINDINGS: Sufficiently high doses of alcohol enhance BZ effects by altered binding of BZ to plasma proteins or other receptor sites. Reports of this occurrence are few, thus, alcohol may not appreciably affect BZ effects. Caffeine counteracts the effects BZ has on performance, amphetamines counteract BZ selectively, and new stimulant antidepressants counteract BZ central antimuscarinic effects, that is, BZ reduction of memory.

INDEX: Benzodiazepines, Triazolam, Alcohol, Caffeine - Psychology - Human

770

AUTHORS: Mattmann, P., Loepfe, M., Scheitlin, T., Schmidlin, D., Gerne, M., Strauch, I., Lehmann, D., and Borbely, A.A.

TITLE: Daytime Residual Effects and Motor Activity After Three Benzodiazepine Hypnotics

REFERENCE: Arzneimittel-Forschung Drug Research, Vol. 32, No. 1, pp. 461-465, 1982.

DRUGS: Triazolam (TM) 0.25, 0.5, 1.0 mg
Nitrazepam (NM) 10 mg
Flunitrazepam (FM) 2.0 mg

SUBJECTS: Human - 18

PROCEDURES: Double-blind crossover design was used. Normal subjects were given the drug, followed by 8 h sleep. Sleepiness following the sleep period was checked by EEG, EMG, and EOG continuous recording. Motor activity, self and investigator ratings, and digit cancellation tests were performed.

FINDINGS: (1) No significant differences in sleep latency were noted. (2) Nighttime motor activity was significantly decreased over placebo but not by one drug more than another. (3) Daytime motor activity was reduced with all drugs except TM (0.25-mg). (4) Residual effects were noted with all three drugs but were significantly reduced with 0.25-mg TM.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

780

AUTHORS: Mitler, M.M., Seidel, W.F., Van den Hoed, J., Greenblatt, D.J., and Dement, W.C.

TITLE: Comparative Hypnotic Effects of Flurazepam, Triazolam, and Placebo: A Long-term Simultaneous Nighttime and Daytime Study

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 1, pp. 2-13, 1984.

DRUGS: Flurazepam (FZP) 30 mg; Triazolam (TZ) 0.5 mg

SUBJECTS: Twenty-one patients with either a primary or secondary diagnosis of psychophysiological insomnia or insomnia associated with personality disorder.

PROCEDURES: Performance testing was done in five 1-h sessions. The battery of tests included the Digit Symbol Substitution Test, Wilkinson Addition Test, and a combined Target Pursuit and Divided Attention Test. The Multiple Sleep Latency Test was given seven times throughout the day.

FINDINGS: Results generally confirm the hypnotic efficacy of both FZP and TZ. At the third week, FZP showed some decreased efficacy, whereas TZ showed no indication of reduced effect even after 5 weeks. Pervasive deterioration in sleep occurred immediately after discontinuation of TZ. A trend occurred toward increased, rather than decreased, alertness for the TZ group. Because of large variability the fact that two TZ subjects had extremely long baseline sleep latencies. This trend did not reach statistical significance. Triazolam tended to improve performance, whereas FZP tended to reduce it.

INDEX: Triazolam, Benzodiazepines - Psychology, Vision - Human

790

AUTHORS: Monti, J.M.

TITLE: Sleep Laboratory and Clinical Studies of the Effects of Triazolam, Flunitrazepam, and Flurazepam in Insomniac Patients

REFERENCE: Methods and Findings of Experimental Clinical Pharmacology, Vol. 3, No. 5, pp. 303-326, 1981.

DRUGS: Triazolam (TM)
Flunitrazepam (FTM)
Flurazepam (FM)

SUBJECTS: Human

PROCEDURES: Review article.

FINDINGS: All three compounds, whether short acting (TM), intermediate-acting (FTM), or long-acting (FM), decreased slow wave activity on the EEG.

COMMENT: This document contains a review of literature summarizing definitions of insomnia and discussing the sleep quality in various age groups, and a discussion of the effects of eight categories of benzodiazepines in short- and long-term use for insomnia.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

800

AUTHORS: Morgan, K., Adam, K., and Oswald, I.

TITLE: Effects of Loprazolam and Triazolam on Psychological Function

REFERENCE: Psychopharmacology, Vol. 82, pp. 386-388, 1984.

DRUGS: Triazolam (TZ) 0.5 mg
Loprazolam (LPM) 0.5 - 1.0 mg

SUBJECTS: Human - 12

PROCEDURES: Double-blind drug administration with the following tests: auditory vigilance, manual dexterity, digit symbol substitution, and card sorting.

FINDINGS: A marginal sleep withdrawal effect was noted with use of TZ. A sleep withdrawal effect also occurred with LZ (1.0 mg). A marginal decrement in manual dexterity test was reported with use of TZ (no data presented).

INDEX: Triazolam, Benzodiazepines - Psychology, Acoustics - Human

810

AUTHORS: Morgan, K. and Oswald, I.

TITLE: Anxiety Caused by a Short-life Hypnotic

REFERENCE: British Medical Journal, Vol. 284, p. 1785, 1982.

DRUGS: Triazolam (TZ) 0.5 mg
Lorprazolam (LZ) 1 mg

SUBJECTS: Human - 21 patients (16 women and 5 men) who were classed as poor sleepers.

PROCEDURES: Each evening, the patients used visual analogue scales to rate how anxious they felt that day.

FINDINGS: Taken at night, LZ was associated with a mean decrease of daytime anxiety; TZ increased anxiety. In their conclusions, the authors assumed that a large dose of TZ each evening was rapidly metabolized but led to a daytime rebound of anxiety. They also felt that a 1-mg dose of TZ might even produce paranoid thinking.

INDEX: Benzodiazepines - Psychology - Human

820

AUTHORS: Muzet, A., Johnson, L.C., and Spinweber, C.L.

TITLE: Benzodiazepine Hypnotics Increase Heart Rate During Sleep

REFERENCE: Naval Health Research Center, 1981, Report 81-16.

DRUGS: Triazolam 0.5 mg
Flurazepam 30 mg

SUBJECTS: Human - 20

PROCEDURES: Subjects who were considered "poor sleepers" (45 min sleep latency for at least 6 months) received placebo for 3 nights; 10 received given the hypnotic and 10 the placebo for 6 nights; and all received the placebo for 2 withdrawal nights. Electrocardiograms were recorded.

FINDINGS: Both drugs elicited significant elevations in heart rate, but by the third day, triazolam-subject heart rates were not significantly different from baseline.

COMMENT: Intravenous administration of these drugs has produced similar findings. There appear to be peripheral effects as well as central sedative effects.

INDEX: Triazolam, Benzodiazepines - Biomedical - Human

830

AUTHORS: Nakamura, M. and Fukushima, H.

TITLE: Effect of Benzodiazepines on Central Serotonergic Neuron Systems

REFERENCE: Psychopharmacology, Vol. 53, pp. 121-126, 1977.

DRUGS: Diazepam
Fludiazepam

SUBJECTS: Mice - 30

PROCEDURES: Intracerebral injection of serotonin induces head twitching in a dose-dependent manner. Benzodiazepines were introduced and twitch differences measured.

FINDINGS: "Benzodiazepines failed to change the uptake of serotonin into the postsynaptosomal fractions from the rat brain." "...the pharmacological action of benzodiazepines is derived at least in part from their activating effect on serotonin receptors."

INDEX: Benzodiazepines - Psychology, Vestibular, Vision, Acoustics - Nonhuman

840

AUTHORS: Nicholson, A.N.

TITLE: Performance Studies with Diazepam and its Hydroxylated Metabolites

REFERENCE: British Journal of Clinical Pharmacology, 1979, Vol. 8, pp. 39S-42S, 1979.

DRUGS: Flurazepam (FM) 30 mg
Nitrazepam (NM) 10 mg
Diazepam (DM) 5, 10 mg
Temazepam (TM) 10, 20, 30 mg
Oxazepam (OM) 15, 30, 45 mg

SUBJECTS: Human - unspecified numbers

PROCEDURES: An adaptive tracking and a visuo-motor task were used.

FINDINGS: Effects of overnight ingestion on performance were:
FM 30 mg - impaired at 16 h
NM 10 mg - impaired at 19 h
DM 5 and 10 mg - not impaired
TM 10, 20, 30 mg - not impaired
OM 15, 30 mg - not impaired
OM 45 mg - impaired at 10 h

INDEX: Benzodiazepines, Temazepam - Vision, Vestibular - Human

850

AUTHORS: Nicholson, A.N.

TITLE: Hypnotics: Rebound Insomnia and Residual Sequelae

REFERENCE: British Journal of Clinical Pharmacology, Vol. 9, pp. 223-225, 1980 (editorial).

DRUGS: Benzodiazepines in general

SUBJECTS: N/A

PROCEDURES: N/A

FINDINGS: Reviews literature supporting and literature refuting the existence of rebound insomnia due to short-acting benzodiazepines (i.e., Triazolam). The author concludes: "There is no reason to believe that the proper use of short-acting hypnotics is detrimental to sleep, either during treatment or on withdrawal, and they maintain their effectiveness over periods of time sufficient for day-to-day clinical practice."

INDEX: Triazolam, Benzodiazepines - Psychology, - Human

860

AUTHORS: Nicholson, A.N.

TITLE: The Use of Short- and Long-acting Hypnotics in Clinical Medicine

REFERENCE: British Journal of Clinical Pharmacology, Vol. 11, pp. 61S-69S, 1981.

DRUGS: Benzodiazepines

SUBJECTS: N/A

PROCEDURE: Review article

FINDINGS: "Hypnotics in which individual elimination half lives do not exceed 24-h are much less likely to lead to impaired performance." Residual impairment of performance has been shown to be significant in long-acting drugs; however, short-acting drugs, including diazepam 10 mg, had little residual effect even a few hours after ingestion.

COMMENT: The quality and effectiveness of benzodiazepines on sleep is also addressed.

INDEX: Triazolam, Benzodiazepines - Vision, Vestibular, Acoustics, Psychology - Human

870

AUTHORS: Nicholson, A.N.

TITLE: Hypnotics and Air Operations

REFERENCE: Defense Technical Information Center, Report AD P002989, Feb 1984, pp. 15-1-15-8.

DRUGS: Benzodiazepines

SUBJECTS: None listed

PROCEDURES: A review.

FINDINGS: Diazepam should not be used more than once in 48 h or more than twice a week. Triazolam and brotizolam may be used daily if essential. All should be given at the lowest dose possible and as infrequently as possible. A 24-h drug-free period should be allowed before starting duty, and may be reduced to 12 h if supervised.

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular, Vision, Acoustics, - Human

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880

AUTHORS: Nicholson, A.N., Roth, T., and Stone, B.M.

TITLE: Hypnotics and Aircrew

REFERENCE: Aviation, Space, and Environmental Medicine, Vol. 56, pp. 299-303, 1985.

DRUGS: Benzodiazepines and other hypnotics

SUBJECTS: N/A

PROCEDURES: Symposium presentation.

FINDINGS: Chronic drug therapy may lead to unwanted effects, whereas simple doses may not. Short half-life drugs are much safer for use in flying duties. Over the age of 45, aviators may require higher doses for effect and thereby increase the risk of adverse effects on performance.

INDEX: Triazolam, Benzodiazepines - Vision, Acoustics, Vestibular, Biomedical, Psychology - Human

890

AUTHORS: Nicholson, A.N. and Stone, B.M.

TITLE: Activity of the Hypnotics, Flunitrazepam and Triazolam in Man

REFERENCE: British Journal of Clinical Pharmacology, Vol. 9, pp. 187-194, 1980.

DRUGS: Triazolam 0.25 and 0.50 mg
Flunitrazepam 0.25 and 0.50 mg

SUBJECTS: Humans - 6 normal noninsomniacs (age 20-30 years)

PROCEDURES: Patients were alcohol-free for 12 h, caffeine free for 1 wk, and did not have daytime naps. Sleep patterns were analyzed by EEGs and performance evaluated by visuomotor coordination. Study time consisted of 2 weeks of performance, measured from 1/2 h to 6 1/2 h after drug or placebo adminstration. During the following 6-week period, subjects received 0.25 or 0.5 mg triazolam or flunitrazepam.

FINDINGS: (1) The drugs had no effect on sleep latency.
(2) Triazolam (0.25 mg) decreased REM sleep the first 6 h but not total sleep time. It had no effect on daytime performance, except when drug was administered during the day.
(3) Triazolam (0.5 mg) produced the same effect on REM sleep as 0.25 mg and increased latency to REM sleep but decreased performance 10 h after ingestion, with no effect after 12 h.

INDEX: Triazolam, Benzodiazepines - Vision, Psychology - Human

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900

AUTHORS: Nicholson, A.N., Stone, B.M., and Pascoe, P.A.

TITLE: Efficacy of Some Benzodiazepines for Daytime Sleep

REFERENCE: British Journal of Clinical Pharmacology, Vol. 10, pp. 459-463, 1980.

DRUGS: Flunitrazepam (FM) 0.25 - 0.50 mg
Brotizolam (BM) 0.3 - 0.6 mg
Triazolam (TM) 0.25 - 0.50 mg

SUBJECTS: Human - 6

PROCEDURES: Healthy subjects' EEGs, EMGs, and EOGs were recorded during daytime sleep.

FINDINGS: "All three drugs improved daytime sleep."
"...suggest that FM may be particularly appropriate for sleep at unusual times."

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular, Vision - Human

910

AUTHORS: Nicholson, A.N., Stone, B.M., and Spencer, M.B.

TITLE: Anxiety Caused by a Short-life Hypnotic

REFERENCE: British Medical Journal, Vol. 284, p. 1785, 1982 (letter to the editor).

DRUGS: Triazolam
Loprazolam

SUBJECTS: N/A

PROCEDURES: Letter to the editor.

FINDINGS: "A reasonable interpretation of the data, despite its shortcomings in design and analysis, is more likely to be that triazolam may lead to daytime anxiety only when unnecessarily high doses are given for unnecessarily long periods of time."

COMMENT: The letter is in response to a previous investigation that reported anxiety was produced by triazolam at a dose of 0.5 mg. The letter asserts that this was probably because this dose is twice that recommended for clinical use in the United Kingdom.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

920

AUTHORS: Novack, G.D. and Owenburg, K.M.

TITLE: Flurazepam and Triazolam: Dose-response and Time-response Evaluation on Cat Sleep

REFERENCE: Electroencephalography and Clinical Neurophysiology, Vol. 57, pp. 277-288, 1984.

DRUGS: Flurazepam (FZP) 1.25, 2.5, and 5.0 mg/kg, i.p.
Triazolam (TZ) 0.01, 0.025, and 0.05 mg/kg, i.p.

SUBJECTS: Female cats (3-4 kg)

PROCEDURES: Stereotaxically implanted depth electrodes (dorsal hippocampus and mesencephalic reticular formation) and cortical electrodes (bilateral suprasylvian gyri and frontal ground). Single- and multiple-dose procedures. Continuous 24-72 h recordings.

FINDINGS: Both of the benzodiazepines depressed the reticular activating system by up to 50% in a dose-related fashion. Flurazepam was effective for 72 h or more; TZ for 24-48 h. Also, FZP was much longer lasting than TZ when administered for 3 days at 24-h intervals. The single- and multiple-dose experiments were conducted to evaluate the procedure for clinical applicability as an animal model of sedative-hypnotic activity.

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular - Nonhuman

930

AUTHORS: Ochs, H.R., Greenblatt, D.J., Arendt, R.M., Hubbel, W., and Shader, I.

TITLE: Pharmacokinetic Noninteraction of Triazolam and Ethanol

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 4, No. 2, pp. 106-107, 1984.

DRUGS: Triazolam 0.5 mg
Ethanol (60 ml vodka)

SUBJECTS: Human - 5

PROCEDURES: A two-way crossover study, which measured serum concentrations.

FINDINGS: Alcohol did not inhibit absorption of triazolam or interfer with its metabolic clearance. "Uncontrolled observations indicated that the combination of triazolam and ethanol produced greater central depression than did triazolam measured alone."

INDEX: Triazolam, Alcohol - Chemistry, - Human

940

AUTHORS: Ogura, C., Nakazawa, K., Majima, K., Nakamura, K., Ueda, H., Umezawa, Y., and Wardell, W.M.

TITLE: Residual Effects of Hypnotics: Triazolam, Flurazepam, and Nitrazepam

REFERENCE: Psychopharmacology, Vol. 68, pp. 61-65, 1980.

DRUGS: Triazolam (TZ) 0.25 and 0.5 mg
Flurazepam (FZP) 15 and 30 mg
Nitrazepam (NZP) 5 and 10 mg

SUBJECTS: Human - 16 healthy volunteers (8 men and 8 women)

PROCEDURES: Sleep and day recordings of EEG, EMG, and EOG.

FINDINGS: Flurazepam and NZP caused residual effects in the morning, afternoon, and evening recording periods the following day. Except for a slight amount in the morning, TZ caused no residual effects the next day.

COMMENT: Data from a 24 h polygram are quantified and presented to indicate the usefulness of polygraphy in evaluating hypnotic drugs.

INDEX: Triazolam, Benzodiazepines - Psychology, Vision - Human

950

AUTHORS: Okawa, K.K. and Allen, G.S.

TITLE: A Clinical Comparison of Triazolam with Placebo and with Secobarbital in Insomniac Patients

REFERENCE: Journal of International Medical Research, Vol. 6, pp. 343-347, 1978.

DRUGS: Triazolam (TZ) 0.5 mg
Secobarbital (SB) 100 mg

SUBJECTS: Human - 76 (outpatient insomniacs)

PROCEDURES: Three different 2-night double-blind crossover trials were carried out. Results were gathered from a patient questionnaire.

FINDINGS: Triazolam was reported to be more preferred and more effective than secobarbital in the treatment of insomnia. No differences were reported between drug treatments with regard to patient's feeling of alertness the next morning.

INDEX: Triazolam - Vestibular, Psychology - Human

960

AUTHORS: Oswald, I. and Adam, K.

TITLE: Benzodiazepines Cause Small Loss of Body Weight

REFERENCE: British Medical Journal, Vol. 281, No. 6247, pp. 1039-1040, 1980.

DRUGS: Nitrazepam (NZP) 5 mg
Lormetazepam (LZPm) 2 mg

SUBJECTS: Humans - 97 volunteers aged 40-68, all complaining of poor sleep

PROCEDURES: The assigning of subjects to treatment was double-blind and evenly distributed in a semi-random design.

FINDINGS: Taking placebo, 12 subjects gained weight and 13 lost. With NZP, 4 gained, 3 were unchanged, and 18 lost weight. On LZPm, 9 gained, 3 were unchanged, and 35 lost weight. Weight loss for both benzodiazepines was significant.

INDEX: Benzodiazepines - Human

970

AUTHORS: Pakes, G.E., Brogden, R.N., Heel, R.C., Speight, T.M., and Avery, G.S.

TITLE: Triazolam: A Review of its Pharmacological Properties and Therapeutic Efficacy in Patients with Insomnia

REFERENCE: Drugs, Vol. 22, pp. 80-110, 1981.

DRUGS: Triazolam (TZ)

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: SIDE EFFECTS: Threefold more residual drowsiness the following morning, dizziness, and dry mouth (at doses 2-4 times clinical). Reports of serious adverse psychological disturbances are presented, which caused the Dutch drug registry to temporarily suspend the sale of TZ. Most of these reports were anecdotal and did not clearly indicate dosage or length of use; other drugs represented confounding variables.

INDEX: Triazolam - Psychology - Human

980

AUTHORS: Pegram, V., Hyde, P., and Linton, P.

TITLE: Chronic Use of Triazolam: The Effects on the Sleep Patterns of Insomniacs

REFERENCE: Journal of International Medical Research, Vol. 8, pp. 224-231, 1980.

DRUGS: Triazolam (TZ) 0.5 mg

SUBJECTS: Human - 6 healthy subjects, ages 41-58 (5 females and 1 male).

PROCEDURES: Objective sleep variables were scored blind by the standard Rechtschaffen and Kales criteria for scoring the EEG/EMG/EOG. Subjective evaluations were also included.

FINDINGS: Acute and chronic TZ administration effectively decreased total wake time and sleep latency, and increased the quality and quantity of sleep. Sleep stages 1 and 2 were significantly altered by the drug but in a positive direction; REM sleep was not significantly changed. Three weeks of TZ usage did not result in tolerance to its hypnotic effects.

INDEX: Triazolam - Psychology - Human

990

AUTHORS: Poldinger, W., Sastre-y-Hernandez, M., and Fichte, K.

TITLE: Study with Lormetazepam as a Hypnotic in General Practice

REFERENCE: Neuropsychobiology, Vol. 9, No. 2-3), pp. 135-138, 1983.

DRUGS: Triazolam (TZ) 0.5 mg
Lormetazepam (LZPm) 0.5 mg

SUBJECTS: Human - 100 patients suffering some form of sleep disturbance

PROCEDURES: Data recordings by the investigator were carried-out twice using a standardized evaluation sheet, once at the beginning and once at the end of treatment.

FINDINGS: Both medications were reported as effective sleep treatments, with TZ being superior overall. The side effects of TZ by case were vertigo (3), headache (1), vomiting (1), disturbances in concentration (2), itching (1), tachycardia (1), tiredness (6), hangover (2), and dyskinesia (1). The side effects recorded for LZPm were headache (1), drowsiness (2), agitation (1), frequent dreams (1), a feeling of finger thickening (1), and tired eyes (1).

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular - Human

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1000

AUTHORS: Purpura, R.P.

TITLE: Approaches in the Evaluation of Hypnotics: Studies with Triazolam

REFERENCE: British Journal of Pharmacology, Vol. 11, pp. 37S-42S, 1981.

DRUGS: Triazolam (TZ)

SUBJECTS: N/A

PROCEDURES: A review of various approaches to research evaluation of triazolam.

FINDINGS: Initial Phase III studies assessed the overall effectiveness of TZ with other drugs used to treat insomnia. The preference technique (patient and physician) is discussed as being one of the most sensitive and effective methods for evaluating short-term efficacy. Studies or evaluations done in conjunction with presurgical patients, hospitalized patients with a variety of illnesses, geriatric patients, mental patients, sleep laboratory, and performance studies, et cetera, are discussed.

INDEX: Triazolam - Psychology - Human

1010

AUTHORS: Rickels, K.

TITLE: Clinical Trials of Hypnotics

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 3, No. 2, pp. 133-139, 1983.

DRUGS: Flurazepam (FZP)
Temazepam (TZP)
Triazolam (TZ)

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: The long half-life drug FZP and the short half-life drug TZ produced similar results in terms of clinical improvement and adverse effects when equivalent dosages were administered. In the present U.S. formulation, TZP appeared to be less effective in sleep latency than the other two compounds. In general, long half-life drugs have a tendency to produce more performance deficits and hangover the following morning than short half-life drugs when used in equivalent dosages. Adverse effects and performance deficits are more dose-related than half-life related.

INDEX: Triazolam, Benzodiazepines, Temazepam - Psychology - Human

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1020

AUTHORS: Rickels, K., Gingrich, R.L., Morris, R.J, Rosenfeld, H., Perloff, M.M., Clark, E.L., and Schilling, A.

TITLE: Triazolam Insomniac Family Practice Patients

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 18, No. 3, pp. 315-324, 1975.

DRUGS: Triazolam 0.5 mg
Secobarbital 100 mg

SUBJECTS: Human - 100

PROCEDURES: A 7-d double-blind study was conducted to compare triazolam and secobarbital. Onset, duration, quality, and residual sleepiness were measured by a symptom checklist and the Clyde Mood Scale.

FINDINGS: Residual sedation with triazolam was more marked than with secobarbital or placebo. Triazolam was preferred over secobarbital by the patients. Triazolam effected a greater reduction in emotional symptoms and was considered an important factor in influencing the response of insomnia to the agent.

INDEX: Triazolam - Psychology - Human

1030

AUTHORS: Roehrs, T., Zorick, F.J., Sicklesteel, J.M., Wittig, R.M., Hartse, K.M., and Roth, T.

TITLE: Effects of Hypnotics on Memory

REFERENCE: Journal of Clinical Pharmacology, Vol. 3, No. 5, pp. 310-313, 1983.

DRUGS: Triazolam (TZ) 0.25 and 0.50 mg
Lorazepam (LZP) 4 mg
Flurazepam (FZP) 30 mg
Secobarbital (SB) 200 mg

SUBJECTS: Humans - 12 healthy male volunteers (21-30 years old)

PROCEDURES: Drugs were administered for 6 consecutive nights to each subject in a modified repeated measure, double-blind, latin square design. In the morning, each subject was tested for recall of 16 items presented during nighttime awakenings.

FINDINGS: With repeated administration of the longer acting FZP, the amnestic effect increased; while repeated administration of the shorter acting drugs, TZ and LZP, did not worsen this effect.

COMMENT: This study confirms the findings of previous studies, which indicated that some BZ possess anterograde amnestic properties. It also provides evidence that the drug-induced amnesia results from a disruption of the memory consolidation process.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1040

AUTHORS: Roth, T., Hartse, K.M., Saab, P.G., Piccione, P.M., and Kramer, M.

TITLE: The Effects of Flurazepam, Lorazepam, and Triazolam on Sleep and Memory

REFERENCE: Psychopharmacology, Vol. 70, pp. 231-237, 1980.

DRUGS: Flurazepam (FM) 30 mg
Lorazepam (LM) 4 mg
Triazolam (TM) 0.5 mg

SUBJECTS: Human - 11

PROCEDURES: A double-blind administration, 2 nights per week, was used for 4 weeks; EEG, EMG, and EOG were recorded. Recall tasks were presented on awakening.

FINDINGS: "Each drug decreased stage 1, increased stage 2, and had no effect on stage 3-4 sleep."...."Post drug recall was significantly decreased in comparison to placebo at night and further decreased in the morning."

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1050

AUTHORS: Roth, T., Kramer, M., and Lutz, T.

TITLE: Intermediate Use of Triazolam: A Sleep Laboratory Study

REFERENCE: Journal of International Medical Research, Vol. 4, pp. 59-63, 1976.

DRUGS: Triazolam (TZ) 0.5 mg

SUBJECTS: Human - 8 (insomniacs)

PROCEDURES: A double-blind study over 22 consecutive nights. Continuous EEG, EOG, and EMG were recorded. The Clyde Mood Scale was administered before and after sleep; a checklist of subjective side effects was also given.

FINDINGS: Triazolam produced a marked reduction in sleep latency and was effective in sleep maintenance. Stage 2 sleep increased with no effect on other stages. "Triazolam showed no systemic effects on pre or post sleep Clyde Mood Scale." Side effects were noted in seven out of eight patients; the most common being dry mouth. Mild residual drowsiness was reported by nearly half of the patients.

INDEX: Triazolam - Psychology - Human

1060

AUTHORS: Roth, T., Kramer, M., and Schwartz, J.

TITLE: Triazolam: A Sleep Laboratory Study of a New Benzodiazepine Hypnotic

REFERENCE: Current Therapeutic Research, Vol. 16, No. 2, pp. 117-123, 1974.

DRUGS: Triazolam (TM) 0.25, 0.5 and 1.0 mg

SUBJECTS: Humans - 12 normal subjects

PROCEDURE Total test time was 9 nights: days 1 and 2 = lab adaptation; days 3 and 4 = baseline data; days 5, 6, and 7 = drug treatment; and days 8 and 9 = recovery. Examined EEG sleep and subjective evaluations by volunteers.

FINDINGS: Because of the limited number of subjects in each group, statistical analysis was not performed at each dose level. Results were as follows: (1) TZ decreased sleep latency; (2) TZ increased stage II sleep duration; (3) TZ initially decreased REM sleep, but REM later returned to normal; (4) rebound insomnia did not occur; and (5) relatively few side effects were reported.

INDEX: Triazolam - Psychology - Human

1070

AUTHORS: Roth, T., Roehrs, T., Wittig, R., and Zorick, F.J.

TITLE: Benzodiazepines and Memory

REFERENCE: British Journal of Clinical Pharmacology, Vol. 18, pp. 45S-49S, 1984.

DRUGS: Triazolam (TM) 0.25 and 0.50 mg
Flurazepam (FM) 30 mg

SUBJECTS: N/A

PROCEDURES: A 16 item-recall lottery test was used 3 h post drug administration. Recall was also tested in the morning, 8 h post drug administration.

FINDINGS: Flurazepam buildup (chronic) increased anterograde amnestic effects. Sleep was more important in the development of a recall block than the drug (consolidation time was important in memory improvement).

INDEX: Triazolam, Benzodiazepine - Psychology - Human

1080

AUTHORS: Roth, T., Roehrs, T.A., and Zorick, F.J.

TITLE: Pharmacology and Hypnotic Efficacy of Triazolam

REFERENCE: Pharmacotherapy, Vol. 3, No. 3, pp. 137-145, 1983.

DRUGS: Triazolam

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: The review discusses the following aspects of triazolam: chemical and physical properties, preparations and dosage, pharmacokinetics, animal pharmacology, hypnotic efficacy, safety, side effects, and paradoxical reactions.

INDEX: Triazolam - Psychology - Human and Nonhuman

1090

AUTHORS: Roth, T., Zorich, F., Sicklesteel, J., and Stepauski, E.

TITLE: Effect of Benzodiazepines on Sleep and Wakefulness

REFERENCE: British Journal Clinical Pharmacology, Vol. 11, pp. 31S-35S, 1981.

DRUGS: Estazolam 2 mg (n = 9)
Triazolam 0.5 mg (n = 8)
Flurazepam 15 mg (n = 9)

SUBJECTS: N/A

PROCEDURES: Review article.

FINDINGS: Various effects of short- and long-acting benzodiazepines on sleep factors and working behavior are presented. Particular emphasis is placed on hypnotic efficacy and the effects on the nature of sleep and daytime performance.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1100

AUTHORS: Safran, A.B., Walser, A., Gauthier, G., and Roth, A.

TITLE: Influence of Central Depressant Drugs on Pupil Function: An Evaluation with the Pupil Cycle Induction Test

REFERENCE: Ophthalmologica, Basel, Vol. 183, pp. 214-219, 1981.

DRUGS: Numerous benzodiazepines and barbiturates at several dose levels

SUBJECTS: Human - 30

PROCEDURES: The pupil cycle induction test (PCIT) was used to measure light-induced pupil oscillations. Decreased response was considered as evidence of anterior visual pathway disturbance.

FINDINGS: Forty-two of the 60 tested eyes demonstrated alterations on the PCIT.

COMMENT: Although depressant drugs appeared to produce alterations in PCIT, dose-effect correlations were not made.

INDEX: Triazolam, Benzodiazepines - Vision - Human

1110

AUTHORS: Scherschlicht, R. and Marias, J.

TITLE: Effects of Oral and Intravenous Midazolam, Triazolam and Flunitrazepam on the Sleep-wakefulness Cycle of Rabbits

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, pp. 29S-35S, 1983.

DRUGS: Midazolam (MM) 1 and 10 mg/kg, i.v. and p.o.
Triazolam (TM) 0.01 and 0.1 mg/kg, i.v. and p.o.
Flunitrazepam (FM) 0.1 and 1 mg/kg, i.v. and p.o.

SUBJECTS: 36 - rabbits

PROCEDURES: Electrodes were implanted on the sensorimotor cortex and the dorsal hippocampus. Muscle electrodes were implanted in the neck, ear, and eyelid musculature. Both REM and non-REM sleep were recorded for 6 h while subjects were under the influence of drugs at various doses.

FINDINGS: (1) At high and low doses, all three drugs affected the sleep wakefulness cycles. (2) The dose-related increase in total sleep time was mainly due to an increase in non-REM sleep. (3) Flunitrazepam had a longer duration of action.

INDEX: Triazolam, Benzodiazepines - Vision, Vestibular, Psychology - Nonhuman

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1120

AUTHORS: Seidel, W.F., Roth, T., Roehrs, T., Zorick, F., and Dement, W.C.

TITLE: Treatment of a 12-hour Shift of Sleep Schedule with Benzodiazepines

REFERENCE: Science, Vol. 224, pp. 1262-1264, 1984.

DRUGS: Triazolam (TZ) 0.5 mg
Flurazepam (FZP) 30 mg

SUBJECTS: TZ (6 males and 2 females, 21-30 years old)
FZP (7 males and 1 female, 20-30 years old)

PROCEDURES: EEG, EMG, and EOG.

FINDINGS: After two baseline 24-h periods, the subjects' sleep was postponed until noon the next day. For the following three 24-h periods, subjects were in bed from 1200 to 2000 and received TZ, FZP, or placebo at bedtime in parallel groups. Placebo subjects showed significant sleep loss after the shift. Active medication reversed this sleep loss. Despite good sleep, FZP-treated subjects appeared the most impaired, of the three groups, on objective assessments of waking function; TZ subjects were the least impaired.

INDEX: Triazolam, Benzodiazepines - Vision, Psychology - Human

1130

AUTHORS: Sethy, V.H. and Harris, D.W.

TITLE: Determination of Biological Activity of Alprazolam, Triazolam and Their Metabolites

REFERENCE: Journal of Pharmaceutical Pharmacology, Vol. 34, pp. 115-116, 1982.

DRUGS: Triazolam (TM)
Alprazolam (AM)
Flunitrazepam (FM)

SUBJECTS: Rats

PROCEDURES: Tritiated FM was given to rats to locate rat brain benzodiazepine receptors. The activity of TM and AM were measured against those preparations.

FINDINGS: "Triazolam and 8-hydroxytriazolam were both potent inhibitors of tritiated FM binding." Both compounds appeared to produce their effect by binding at benzodiazepine receptor sites.

INDEX: Triazolam, Benzodiazepines - Chemistry, Psychology - Nonhuman

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1140

AUTHORS: Shader, R.I.

TITLE: New Benzodiazepines: Temazepam, Halazepam, Alprazolam, and Triazolam

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 2, No. 3, pp. 159-160, 1982.

DRUGS: New benzodiazepines

SUBJECTS: N/A

PROCEDURES: Editorial.

FINDINGS: "Triazolam holds promise as a truly short-acting hypnotic that is essentially nonaccumulating and with minimal risk of residual daytime effects following nighttime dosage." Discontinuation of any benzodiazepine after long-term use may lead to rebound insomnia.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1150

AUTHORS: Shader, R.I. and Greenblatt, D.J.

TITLE: Triazolam and Anterograde Amnesia: All is Not Well in the Z-zone

REFERENCE: Journal of Clinical Psychopharmacology, Vol. 3, No. 5, p. 273, 1983.

DRUGS: Triazolam (TZ)

SUBJECTS: N/A

PROCEDURES: Four brief case observations of significant memory loss due to one-time use of TZ.

FINDINGS: The report briefly describes the events surrounding the loss of memory (dramatic) of four different people who used TZ one time to ensure sleep.

INDEX: Triazolam - Psychology, Vestibular - Vision - Human

1160

AUTHORS: Spinweber, C.L. and Johnson, L.C.

TITLE: Effect of Triazolam (0.5 mg) on Sleep, Performance, Memory, and Arousal Threshold

REFERENCE: Psychopharmacology, Vol. 76, pp. 5-12, 1982.

DRUGS: Triazolam (TZ) 0.5 mg

SUBJECTS: Human - 20

PROCEDURES: Nighttime arousal was at 1.5, 3, and 5 h post administration. The following tests were used: four choice reaction time, digit symbol substitution, and Williams Word memory card sorting task.

FINDINGS: Prior to TZ administration, learning was unimpaired. Learning from nighttime arousal was impaired (anterograde amnesia). Performance was impaired if awakened (post TZ administration) at 1.5, 3, and 5 h. No "rebound insomnia" was reported with TZ.

INDEX: Triazolam - Psychology - Human

1170

AUTHORS: Spinweber, C.L. and Johnson, L.C.

TITLE: Psychopharmacological Techniques for Optimizing Human Performance

REFERENCE: Naval Health Research Center, 1983, Report No. 83-11.

DRUGS: Triazolam 0.25 - 1.0 mg
L-Tryptophan 3 - 4 g

SUBJECTS: Human - 20

PROCEDURES: "Poor sleepers" were given placebo for 3 nights: 10 subjects were given the drug 6 nights and all were given placebo for 2 nights post study. Psychologic performance batteries were administered, and EEGs monitored.

FINDINGS: Triazolam: Sleep latency was reduced the first night. Nighttime testing produced performance decrements. Testing at 8.25 h post administration produced no performance decrement.

L-Tryptophan: Sleep latency was reduced only after 3 consecutive administration nights. Nighttime testing and testing at 8.25 h post dose produced no performance decrement.

COMMENT: This appears to be a well designed comparative study.

INDEX: Triazolam, L-Tryptophan - Psychology - Human

1180

AUTHORS: Stone, B.M.

TITLE: Pencil and Paper Tests - Sensitivity to Psychotropic Drugs

REFERENCE: British Journal of Clinical Pharmacology, Vol. 18, pp. 15S-20S, 1984.

DRUGS: Triazolam

SUBJECTS: Human - 7

PROCEDURES: Constant plasma concentrations of triazolam were maintained via a rectal infusion pump. Two- and-six letter cancellation, logic, mental arithmetic, symbol copying, digit symbol substitution, and concept identity tests were given.

FINDINGS: Paper and pencil tests are simple to administer and are useful to detect impaired performance. Cancellation, mental arithmetic, and digit symbol substitution tests, appeared to be the most sensitive.

INDEX: Triazolam - Psychology - Human

1190

AUTHORS: Subhan, Z. and Hindmarch, I.

TITLE: Assessing Residual Effects of Benzodiazepines on Short Term Memory

REFERENCE: Pharmaceutics and Medicine, Vol. 1, pp. 27-32, 1984.

DRUGS: Lormetazepam (LM) 1 mg
Triazolam (TM) 0.25 mg
Nitrazepam (NM) 5 mg
Temazepam (TEM) 20 mg
Flurazepam (FM) 15 mg

SUBJECTS: Human - 12

PROCEDURES: Double-blind crossover study. Short-term memory measured after nighttime administration (12 h post administration).

FINDINGS: Short-term memory was significantly impaired by TM, NM, TEM, and FM; LM had no significant effect.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1200

AUTHORS: Sundaresan, P.R., Wardell, W.M., Weintraub, M., and Lasagna, L.

TITLE: Methodology for Demonstrating Sustained Efficacy of Hypnotics: A Comparative Study of Triazolam and Flurazepam

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 25, No. 4, pp. 391-398, 1979.

DRUGS: Triazolam (TZ) 0.6 mg
Flurazepam (FZP) 30 mg

SUBJECTS: Human - 37 insomniac patients (20-60 years old)

PROCEDURES: The hypnotic effect of the medication was evaluated by a patient interview each morning. The data were collected by a trained person using a sleep questionnaire, which included adverse effects. The double-blind study was conducted over 7 consecutive nights.

FINDINGS: At this dose, TZ was an effective hypnotic by all usual subjective measures and did not produce appreciable hangover; FZP performed similarly. Both TZ and FZP showed sustained efficacy at the above dosages for 1 week.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1210

AUTHORS: Sunshine, A.

TITLE: Comparison of the Hypnotic Activity of Triazolam, Flurazepam Hydrochloride, and Placebo

REFERENCE: Clinical Pharmacology and Therapeutics, Vol. 17, No. 5, pp. 573-577, 1975.

DRUGS: Triazolam (TM) 0.4 and 0.8 mg
Flurazepam (FM) 15 and 30 mg

SUBJECTS: Human - 25 (insomniacs)

PROCEDURES: This was a 5-night double-blind crossover study using insomniacs. Subjective ratings and observations were made.

FINDINGS: Very few adverse effects were reported. All medications were reported to be superior to the placebo in inducing sleep. Only TM was reported to be faster than the placebo in reducing onset of sleep.

COMMENT: The study was a purely subjective survey, except for the observations during sleep.

INDEX: Triazolam, Benzodiazepines - Psychology - Human

1220

AUTHORS: van der Kroef, C.

TITLE: Reactions to Triazolam

REFERENCE: Lancet, Vol. 2, No. 8141, p. 526, 1979 (letter to the editor).

DRUGS: Triazolam (TZ)

SUBJECTS: N/A

PROCEDURES: N/A

FINDINGS: The letter describes a psychiatrist's observations concerning the effects of TZ. He describes the following symptoms: severe malaise, depersonalization and derealization, paranoid reactions, acute and chronic anxiety, continuous fear of going insane, depression and deterioration of existing depressions, hyperesthesia (especially for sound but also of smell, taste, and light), sometimes hypoesthesia for the same stimuli, nightmares, restlessness, inability to concentrate, impaired motor function, blurred vision, et cetera.

INDEX: Triazolam - Psychology, Vision - Human

1230

AUTHORS: Walsh, J.K., Muehlbach, M.J., and Schweitzer, P.K.

TITLE: Acute Administration of Triazolam for the Daytime Sleep of Rotating Shift Workers

REFERENCE: Sleep, Vol. 7, No. 3, pp. 223-229, 1984.

DRUGS: Triazolam 0.5 mg, p.o.

SUBJECTS: Human - 10

PROCEDURES: Double-blind crossover study of rotating-shift workers who were measured by polysomnography during disrupted cycles of sleep. Card sorting and digit symbol substitution tests (DSST) were administered.

FINDINGS: Triazolam significantly improved sleep efficiency and total sleep time relative to placebo, primarily by promoting maintenance of sleep. Post-sleep DSST measurements indicated a marked decrease in performance, suggesting that doses lower than 0.5 mg should be used.

COMMENT: This is one of many studies indicating decreased performance at higher doses of triazolam.

INDEX: Triazolam - Psychology - Human

1240

AUTHORS: Wang, R.I.H., Wilbur, M., and Hieb, E.

TITLE: Determining Optimum Dose and Acute Tolerance of Triazolam

REFERENCE: Journal of International Medical Research, Vol. 5, pp. 184-190, 1977.

DRUGS: Triazolam 0.5 - 3.0 mg

SUBJECTS: Human - 14

PROCEDURES: Drug given in 0.5-mg increments from 1.0 mg to maximal tolerance (3.0 mg) as indicated by undesirable side effects. The objective measurement of ability to resume sleep after stimulus was recorded.

FINDINGS: Observed decreases in sleep induction time and increases in duration were reported. Ataxia, dry mouth, and drowsiness were noted.

INDEX: Triazolam - Psychology - Human

1250

AUTHORS: Wincor, M.Z.

TITLE: Insomnia and the New Benzodiazepines

REFERENCE: Clinical Pharmacology, Vol. 1, pp. 425-432, 1982.

DRUGS: Temazepam (TZP) 30 mg
Triazolam (TZ) 0.25 - 0.5 mg

SUBJECTS: N/A

PROCEDURES: A drug review.

FINDINGS: The review considers the following aspects of the drugs TZ and TZP: sleep (EEG, EMG, EOG), insomnia (circadian rhythm and jet lag), other types of testing for sleep effectiveness, chemical descriptions, pharmacokinetics, and associated side effects.

INDEX: Triazolam, Temazepam - Vestibular - Vision - Human

1260

AUTHORS: Ziegler, W.H., Schalch, E., Leishman, B., and Eckert, M.

TITLE: Comparison of the Effects of Intravenously Administered Midazolam, Triazolam and Their Hydroxy Metabolites

REFERENCE: British Journal of Clinical Pharmacology, Vol. 16, pp. 63S-69S, 1983.

DRUGS: Midazolam 15 mg, i.v.
Triazolam 0.25 mg and 1.0 mg, i.v.

SUBJECTS: Human - 6

PROCEDURES: This was a randomized crossover study in which subjects received drugs and drug metabolites. Psychometric testing, self rating, and investigator assessment were done at intervals during a 24-h period.

FINDINGS: A sedative effect was marked for triazolam at the 1-mg dose. At 0.25 mg, triazolam was roughly equivalent to 15 mg midazolam in terms of sedation, but the effect of triazolam was weaker. Psychometric testing at 1 mg triazolam showed a profound effect. Triazolam (0.25 mg) and midazolam (15 mg) disturbed performance, but the disturbance due to triazolam was of much shorter duration, 1.5 h.

INDEX: Triazolam, Benzodiazepines - Psychology, Vestibular - Human

SUBJECT INDEX

L-Tryptophan	1180
Vestibular	30,190,220,230,240,270,290,460,470,520,590,690,730,830, 840,860,870,880,900,920,950,990,1110,1150,1250,1260
Vision	110,120,220,230,240,290,400,440,460,490,520,530,570,620, 630,640,690,780,830,840,860,870,880,890,900,940, 1100,1110,1120,1150,1220,1250

Other Related NAMRL Publications*

Murdoch, D.M., Lentz, J.M., Reams, G.G., and DeJohn, C.A., Triazolam-Performance Side Effects: Vestibular, Musculoskeletal, and Complex Performance Tests, NAMRL-1327, Naval Aerospace Medical Research Laboratory, Pensacola, FL, March 1987. (AD A180 934)

Thornton, M. and Morey, W.A., Selected Aspects of Triazolam in Relation to Aviator Performance in Naval Flight Operations, NAMRL TM87-1, Naval Aerospace Medical Research Laboratory, Pensacola, FL, November 1987. (AD A189 322)

* Available from DTIC, Cameron Station, Alexandria, VA 22314 (Phone: (C) 202/274-7633 or (AV) 284-7633).